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		(71) Applicant (for all designated States except US): HUMAN GENOME SCIENCES, INC. [US/US]; 9410 Key West Avenue, Rockville, MD 20850 (US).	
		(72) Inventors; and	
		(75) Inventors/Applicants (for US only): FISCHER, Carrie, L. [US/US]; 5810 Hall Street, Burke, VA 22015 (US). ROSEN, Craig, A. [US/US]; 22400 Rolling Hill Road, Laytonsville, MD 20882 (US). SOPPET, Daniel, R. [US/US]; 15050 Stillfield Place, Centreville, VA 22020 (US). RUBEN, Steven, M. [US/US]; 18528 Heritage Hills Drive, Olney, MD 20832 (US). KYAW, Hla [MM/US]; 520 Sugarbush Circle, Frederick, MD 21703 (US). LI, Yi [CN/US]; 1247 Lakeside #3034, Sunnyvale, CA 94086 (US). ZENG, ZhiZhen [CN/US]; 13950 Saddlevue Drive, Gaithersburg, MD 20878 (US). LAFLEUR, David, W. [US/US]; 1615 Q. Street, N.W. #807, Washington, DC 20009 (US). MOORE, Paul, A. [GB/US]; Apartment 104, 1908 Holly Ridge Drive, Mclean, VA 22102 (US). SHI, Yanggu [CN/US]; 437 West Side Drive, Gaithersburg, MD 20878 (US). OLSEN, Henrik, S. [DK/US]; 182 Kendrick Place #24, Gaithersburg, MD 20878 (US). EBNER, Reinhard [DE/US]; 9906 Shelburne Terrace #316, Gaithersburg, MD 20878 (US). BREWER, Laurie, A. [US/US]; 14920 Mt. Nebo Road, Poolesville, MD 20837 (US).	
		(74) Agents: BROOKES, A., Anders et al.; Human Genome Sciences, Inc., 9410 Key West Avenue, Rockville, NMD 20850 (US).	
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(54) Title: 123 HUMAN SECRETED PROTEINS

(57) Abstract

The present invention relates to novel human secreted proteins and isolated nucleic acids containing the coding regions of the genes encoding such proteins. Also provided are vectors, host cells, antibodies, and recombinant methods for producing human secreted proteins. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating disorders related to these novel human secreted proteins.

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## 123 Human Secreted Proteins

### *Field of the Invention*

This invention relates to newly identified polynucleotides and the polypeptides encoded by these polynucleotides, uses of such polynucleotides and polypeptides, and  
5 their production.

### *Background of the Invention*

Unlike bacterium, which exist as a single compartment surrounded by a membrane, human cells and other eucaryotes are subdivided by membranes into many functionally distinct compartments. Each membrane-bounded compartment, or  
10 organelle, contains different proteins essential for the function of the organelle. The cell uses "sorting signals," which are amino acid motifs located within the protein, to target proteins to particular cellular organelles.

One type of sorting signal, called a signal sequence, a signal peptide, or a leader sequence, directs a class of proteins to an organelle called the endoplasmic reticulum  
15 (ER). The ER separates the membrane-bounded proteins from all other types of proteins. Once localized to the ER, both groups of proteins can be further directed to another organelle called the Golgi apparatus. Here, the Golgi distributes the proteins to vesicles, including secretory vesicles, the cell membrane, lysosomes, and the other organelles.

20 Proteins targeted to the ER by a signal sequence can be released into the extracellular space as a secreted protein. For example, vesicles containing secreted proteins can fuse with the cell membrane and release their contents into the extracellular space - a process called exocytosis. Exocytosis can occur constitutively or after receipt of a triggering signal. In the latter case, the proteins are stored in secretory vesicles (or  
25 secretory granules) until exocytosis is triggered. Similarly, proteins residing on the cell membrane can also be secreted into the extracellular space by proteolytic cleavage of a "linker" holding the protein to the membrane.

Despite the great progress made in recent years, only a small number of genes encoding human secreted proteins have been identified. These secreted proteins include  
30 the commercially valuable human insulin, interferon, Factor VIII, human growth hormone, tissue plasminogen activator, and erythropoietin. Thus, in light of the pervasive role of secreted proteins in human physiology, a need exists for identifying and characterizing novel human secreted proteins and the genes that encode them. This knowledge will allow one to detect, to treat, and to prevent medical disorders by using  
35 secreted proteins or the genes that encode them.

### *Summary of the Invention*

The present invention relates to novel polynucleotides and the encoded polypeptides. Moreover, the present invention relates to vectors, host cells, antibodies, and recombinant methods for producing the polypeptides and polynucleotides. Also provided are diagnostic methods for detecting disorders related to the polypeptides, and therapeutic methods for treating such disorders. The invention further relates to screening methods for identifying binding partners of the polypeptides.

### *Detailed Description*

#### **Definitions**

The following definitions are provided to facilitate understanding of certain terms used throughout this specification.

In the present invention, "isolated" refers to material removed from its original environment (e.g., the natural environment if it is naturally occurring), and thus is altered "by the hand of man" from its natural state. For example, an isolated polynucleotide could be part of a vector or a composition of matter, or could be contained within a cell, and still be "isolated" because that vector, composition of matter, or particular cell is not the original environment of the polynucleotide.

In the present invention, a "secreted" protein refers to those proteins capable of being directed to the ER, secretory vesicles, or the extracellular space as a result of a signal sequence, as well as those proteins released into the extracellular space without necessarily containing a signal sequence. If the secreted protein is released into the extracellular space, the secreted protein can undergo extracellular processing to produce a "mature" protein. Release into the extracellular space can occur by many mechanisms, including exocytosis and proteolytic cleavage.

As used herein, a "polynucleotide" refers to a molecule having a nucleic acid sequence contained in SEQ ID NO:X or the cDNA contained within the clone deposited with the ATCC. For example, the polynucleotide can contain the nucleotide sequence of the full length cDNA sequence, including the 5' and 3' untranslated sequences, the coding region, with or without the signal sequence, the secreted protein coding region, as well as fragments, epitopes, domains, and variants of the nucleic acid sequence. Moreover, as used herein, a "polypeptide" refers to a molecule having the translated amino acid sequence generated from the polynucleotide as broadly defined.

In the present invention, the full length sequence identified as SEQ ID NO:X was often generated by overlapping sequences contained in multiple clones (contig



analysis). A representative clone containing all or most of the sequence for SEQ ID NO:X was deposited with the American Type Culture Collection ("ATCC"). As shown in Table 1, each clone is identified by a cDNA Clone ID (Identifier) and the ATCC Deposit Number. The ATCC is located at 10801 University Boulevard,  
5 Manassas, Virginia 20110-2209, USA. The ATCC deposit was made pursuant to the terms of the Budapest Treaty on the international recognition of the deposit of microorganisms for purposes of patent procedure.

A "polynucleotide" of the present invention also includes those polynucleotides capable of hybridizing, under stringent hybridization conditions, to sequences contained  
10 in SEQ ID NO:X, the complement thereof, or the cDNA within the clone deposited with the ATCC. "Stringent hybridization conditions" refers to an overnight incubation at 42°C in a solution comprising 50% formamide, 5x SSC (750 mM NaCl, 75 mM sodium citrate), 50 mM sodium phosphate (pH 7.6), 5x Denhardt's solution, 10% dextran sulfate, and 20 µg/ml denatured, sheared salmon sperm DNA, followed by washing the  
15 filters in 0.1x SSC at about 65°C.

Also contemplated are nucleic acid molecules that hybridize to the polynucleotides of the present invention at lower stringency hybridization conditions. Changes in the stringency of hybridization and signal detection are primarily accomplished through the manipulation of formamide concentration (lower percentages  
20 of formamide result in lowered stringency); salt conditions, or temperature. For example, lower stringency conditions include an overnight incubation at 37°C in a solution comprising 6X SSPE (20X SSPE = 3M NaCl; 0.2M NaH<sub>2</sub>PO<sub>4</sub>; 0.02M EDTA, pH 7.4), 0.5% SDS, 30% formamide, 100 µg/ml salmon sperm blocking DNA; followed by washes at 50°C with 1XSSPE, 0.1% SDS. In addition, to achieve even  
25 lower stringency, washes performed following stringent hybridization can be done at higher salt concentrations (e.g. 5X SSC).

Note that variations in the above conditions may be accomplished through the inclusion and/or substitution of alternate blocking reagents used to suppress background in hybridization experiments. Typical blocking reagents include  
30 Denhardt's reagent, BLOTTO, heparin, denatured salmon sperm DNA, and commercially available proprietary formulations. The inclusion of specific blocking reagents may require modification of the hybridization conditions described above, due to problems with compatibility.

Of course, a polynucleotide which hybridizes only to polyA+ sequences (such  
35 as any 3' terminal polyA+ tract of a cDNA shown in the sequence listing), or to a

complementary stretch of T (or U) residues, would not be included in the definition of "polynucleotide," since such a polynucleotide would hybridize to any nucleic acid molecule containing a poly (A) stretch or the complement thereof (e.g., practically any double-stranded cDNA clone).

5           The polynucleotide of the present invention can be composed of any polyribonucleotide or polydeoxribonucleotide, which may be unmodified RNA or DNA or modified RNA or DNA. For example, polynucleotides can be composed of single- and double-stranded DNA, DNA that is a mixture of single- and double-stranded regions, single- and double-stranded RNA, and RNA that is mixture of single- and double-stranded regions, hybrid molecules comprising DNA and RNA that may be  
10           single-stranded or, more typically, double-stranded or a mixture of single- and double-stranded regions. In addition, the polynucleotide can be composed of triple-stranded regions comprising RNA or DNA or both RNA and DNA. A polynucleotide may also contain one or more modified bases or DNA or RNA backbones modified for stability  
15           or for other reasons. "Modified" bases include, for example, tritylated bases and unusual bases such as inosine. A variety of modifications can be made to DNA and RNA; thus, "polynucleotide" embraces chemically, enzymatically, or metabolically modified forms.

          The polypeptide of the present invention can be composed of amino acids joined  
20           to each other by peptide bonds or modified peptide bonds, i.e., peptide isosteres, and may contain amino acids other than the 20 gene-encoded amino acids. The polypeptides may be modified by either natural processes, such as posttranslational processing, or by chemical modification techniques which are well known in the art. Such modifications are well described in basic texts and in more detailed monographs,  
25           as well as in a voluminous research literature. Modifications can occur anywhere in a polypeptide, including the peptide backbone, the amino acid side-chains and the amino or carboxyl termini. It will be appreciated that the same type of modification may be present in the same or varying degrees at several sites in a given polypeptide. Also, a given polypeptide may contain many types of modifications. Polypeptides may be  
30           branched, for example, as a result of ubiquitination, and they may be cyclic, with or without branching. Cyclic, branched, and branched cyclic polypeptides may result from posttranslation natural processes or may be made by synthetic methods. Modifications include acetylation, acylation, ADP-ribosylation, amidation, covalent attachment of flavin, covalent attachment of a heme moiety, covalent attachment of a  
35           nucleotide or nucleotide derivative, covalent attachment of a lipid or lipid derivative, covalent attachment of phosphatidylinositol, cross-linking, cyclization, disulfide bond formation, demethylation, formation of covalent cross-links, formation of cysteine,

formation of pyroglutamate, formylation, gamma-carboxylation, glycosylation, GPI anchor formation, hydroxylation, iodination, methylation, myristoylation, oxidation, pegylation, proteolytic processing, phosphorylation, prenylation, racemization, selenoylation, sulfation, transfer-RNA mediated addition of amino acids to proteins such as arginylation, and ubiquitination. (See, for instance, PROTEINS - STRUCTURE AND MOLECULAR PROPERTIES, 2nd Ed., T. E. Creighton, W. H. Freeman and Company, New York (1993); POSTTRANSLATIONAL COVALENT MODIFICATION OF PROTEINS, B. C. Johnson, Ed., Academic Press, New York, pgs. 1-12 (1983); Seifter et al., Meth Enzymol 182:626-646 (1990); Rattan et al., Ann NY Acad Sci 663:48-62 (1992).)

"SEQ ID NO:X" refers to a polynucleotide sequence while "SEQ ID NO:Y" refers to a polypeptide sequence, both sequences identified by an integer specified in Table 1.

"A polypeptide having biological activity" refers to polypeptides exhibiting activity similar, but not necessarily identical to, an activity of a polypeptide of the present invention, including mature forms, as measured in a particular biological assay, with or without dose dependency. In the case where dose dependency does exist, it need not be identical to that of the polypeptide, but rather substantially similar to the dose-dependence in a given activity as compared to the polypeptide of the present invention (i.e., the candidate polypeptide will exhibit greater activity or not more than about 25-fold less and, preferably, not more than about tenfold less activity, and most preferably, not more than about three-fold less activity relative to the polypeptide of the present invention.)

## **Polynucleotides and Polypeptides of the Invention**

### **FEATURES OF PROTEIN ENCODED BY GENE NO: 1**

This gene maps to chromosome 12, and therefore, may be used as a marker in linkage analysis for chromosome 12.

This gene is expressed primarily in cerebellum.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, damage to the cerebellum or additional CNS tissues caused by insults

such as trauma or ischemia. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system (CNS), expression of this gene at  
5 significantly higher or lower levels may be routinely detected in certain tissues (e.g., neural cells and tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an  
10 individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:150 as residues: Pro-7 to Cys-21, Leu-25 to Ser-30.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states and behavioural disorders such as Alzheimers Disease, Parkinsons  
15 Disease, Huntingtons Disease, Tourette Syndrome, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the  
20 developing embryo - particularly those associated with neuromuscular junctions, sexually-linked disorders, or disorders of the cardiovascular system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tumors and tissues. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through  
25 sequence databases. Some of these sequences are related to SEQ ID NO:11 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a  
30 nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1868 of SEQ ID NO:11, b is an integer of 15 to 1882, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:11, and where b is greater than or equal to a + 14.

35

## FEATURES OF PROTEIN ENCODED BY GENE NO: 2

This gene is expressed primarily in PHA stimulated T-cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, autoimmune disease. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., immune cells and tissue, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of a variety of immune system disorders. Expression of this gene product in tonsils indicates a role in the regulation of the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer e.g., by boosting immune responses. Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, and leukemia. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tumors and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tumors and tissues. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:12 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly,

preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1576 of SEQ ID NO:12, b is an integer of 15 to 1590, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:12, and where b is greater than or equal to a + 14.

### FEATURES OF PROTEIN ENCODED BY GENE NO: 3

The translation product of this gene was shown to have homology to the human retrovirus-related reverse transcriptase pseudogene (See Genbank Accession No. pirlA25313IGNHUL1). In specific embodiments, polypeptides of the invention comprise the amino acid sequence:

STHASVQKKDLTKFSAHSWLKKKKTFRKMIMEEIFLNLIKNIYKSPYSQCNT  
(SEQ ID NO:289), VRSEKGFDKIQCPFMVK (SEQ ID NO:290),  
FSKPSSYKTYIPKINLHF YILLMNIWETIKIVPLNNCFTKMNYLGI (SEQ ID  
NO:291), KKETKLSLFANDMI (SEQ ID NO:292), and/or  
SPLLFNILLEVLSSAVRKEKELK (SEQ ID NO:293). An additional embodiment is the polynucleotides encoding these polypeptides.

This gene is expressed primarily in PHA activated T cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, inflammation and autoimmune diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., immune cells and tissue, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:152 as residues: Ile-14 to Thr-24.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of a variety of immune system disorders. Expression of this gene product in tonsils indicates a role in

the regulation of the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer e.g., by

5 boosting immune responses. Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, and leukemia. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy

10 targets for the above listed tumors and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Alternatively, the homology to a reverse transcriptase human gene may implicate this gene as providing utility in the understanding of host-viral interactions, particularly

15 those involving retroviruses and other integration-dependent viruses. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:13 and may have been

20 publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1359 of

25 SEQ ID NO:13, b is an integer of 15 to 1373, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:13, and where b is greater than or equal to a + 14.

#### 30 FEATURES OF PROTEIN ENCODED BY GENE NO: 4

The translation product of this gene shares sequence homology with npdcf-1 which is thought to be important in promoting the survival of bi-potential glial progenitor cells (See Genbank Accession No. gil456107). In specific embodiments,

35 polypeptides of the invention comprise the amino acid sequence:

LRRPSTPLRRPWLHLQLPRISLGDQRLAQAEMYHYQHQRQQMLSLERHKEPP  
KELDTALRMRRMRTETS RCTSARAWPRPGKWRCATICSTTPHCPRPC

RPPAHLRH CHDLEADRRPLAPR (SEQ ID NO:294), RATQGAGHGSSDEENED  
 GDFTVYECPGM APTGEMEVNRHLFD HAALSAPLPAPSSPLALP (SEQ ID  
 NO:295), KAEYATAK ALATPAATPD LAWGPAPGTERGDVPLPAPTATDV  
 VPGAA (SEQ ID NO:296), SAEM YHYQHQRQQML (SEQ ID NO:297),  
 5 LERHKEPPKEL (SEQ ID NO:298), AKCPPGA HACGP (SEQ ID NO:299),  
 PVHMSPLEP (SEQ ID NO:300), WCRLQREIRLTQ (SEQ ID NO:301),  
 SSDEENEDGDFTVYECPG (SEQ ID NO:302), APTGEMEVNR (SEQ ID NO:303),  
 and/or CPGSLDCALK (SEQ ID NO:304). Additional embodiments is the  
 polynucleotides encoding these polypeptides.

10 It has been discovered that this gene is expressed primarily in cerebellum and  
 synovial sarcoma and to a lesser extent in several other cancer cell lines.

Therefore, polynucleotides and polypeptides of the invention are useful as  
 reagents for differential identification of the tissue(s) or cell type(s) present in a  
 biological sample and for diagnosis of diseases and conditions which include, but are  
 15 not limited to, tumors characterized by cells of a relatively undifferentiated state, and/or  
 neural tumors. Similarly, polypeptides and antibodies directed to these polypeptides are  
 useful in providing immunological probes for differential identification of the tissue(s)  
 or cell type(s). For a number of disorders of the above tissues or cells, particularly of  
 the synovial fluid, prostate, breast and uterus, expression of this gene at significantly  
 20 higher or lower levels may be routinely detected in certain tissues (e.g., neural cells and  
 tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma,  
 urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an  
 individual having such a disorder, relative to the standard gene expression level, i.e.,  
 the expression level in healthy tissue or bodily fluid from an individual not having the  
 25 disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID  
 NO:153 as residues: Pro-6 to Arg-11, Glu-52 to Gly-59.

The tissue distribution and homology to npdcf-1 indicates that polynucleotides  
 and polypeptides corresponding to this gene are useful for diagnosing and treating  
 tumors that contain relatively undifferentiated cells. In addition, The tissue distribution  
 30 indicates that polynucleotides and polypeptides corresponding to this gene are useful  
 for the detection/treatment of neurodegenerative disease states and behavioural disorders  
 such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette  
 Syndrome, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder,  
 panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors,  
 35 including disorders in feeding, sleep patterns, balance, and preception. In addition, the  
 gene or gene product may also play a role in the treatment and/or detection of  
 developmental disorders associated with the developing embryo, sexually-linked



disorders, or disorders of the cardiovascular system. Alternatively, the expression of this gene product in synovium would suggest a role in the detection and treatment of disorders and conditions affecting the skeletal system, in particular the connective tissues (e.g., arthritis, trauma, tendonitis, chondromalacia and inflammation). Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tumors and tissues. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:14 and may have been publicly available prior to conception of the present invention.

Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1128 of SEQ ID NO:14, b is an integer of 15 to 1142, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:14, and where b is greater than or equal to a + 14.

#### FEATURES OF PROTEIN ENCODED BY GENE NO: 5

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This gene is expressed primarily in colon, pituitary, and to a lesser extent in fetal lung and fibrosarcoma.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, endocrine disorders effecting the Gut/ pituitary/hypothalamic axis. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the digestive system and regulation of feeding, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., gastrointestinal tissue, endocrine tissue, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a

sequence shown in SEQ ID NO:154 as residues: Asn-26 to Cys-32, Cys-100 to Leu-112, Cys-128 to Ser-135.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for treating disorders related to the intake and utilization of food since this gene is expressed in the digestive tract and a CNS site involved in regulation of weight homeostasis. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:15 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1020 of SEQ ID NO:15, b is an integer of 15 to 1034, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:15, and where b is greater than or equal to a + 14.

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#### FEATURES OF PROTEIN ENCODED BY GENE NO: 6

The translation product of this gene shares sequence homology with Cortical granule lectin which is thought to be important in blocking polyspermy during fertilization of the egg (See Genbank Accession No. gnl|PID|e1181610). Preferred polypeptides comprise the following amino acid sequence: RSCKEIKD (SEQ ID NO:305), GGGWTLVASVHEN (SEQ ID NO:306), ADYPEGDGNWANYNTFGSA (SEQ ID NO:307), ATSDDYKNPGYYDI (SEQ ID NO:308), CIGGGGYFPEA (SEQ ID NO:309), and/or EITEAAVLLFY (SEQ ID NO:310). Also preferred are the polynucleotides encoding these polypeptides.

This gene is expressed primarily in benign and metastatic colon, and to a lesser extent in HEL cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cancer, or inflammatory conditions of the colon. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological

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probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the digestive system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., gastrointestinal tissue, and proliferating, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:155 as residues: Arg-15 to Ser-33, Pro-35 to Cys-41.

The tissue distribution and homology to cortical granule lectins indicates that polynucleotides and polypeptides corresponding to this gene are useful for treating disorders of the colon. These may include diseases related to damage or chronic inflammation as well as tumors of the colon. The product may also be useful for the identification of colon cancer metastasis and, as a secreted protein, may have diagnostic and prognostic applications. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tumors and tissues. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:16 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1184 of SEQ ID NO:16, b is an integer of 15 to 1198, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:16, and where b is greater than or equal to a + 14.

## **FEATURES OF PROTEIN ENCODED BY GENE NO: 7**

This gene is expressed primarily in eight week human embryos.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, fetal and/or developmental abnormalities. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes

for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the developing fetus, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., developing and/or differentiating cells or tissue, and cancerous and wounded  
5 tissues) or bodily fluids (e.g., amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides  
10 corresponding to this gene are useful for detecting embryonic abnormalities. Expression within embryonic tissue and other cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Many polynucleotide  
15 sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:17 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably  
20 excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1433 of SEQ ID NO:17, b is an integer of 15 to 1447, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:17, and where b is greater than or equal to a + 14.

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## FEATURES OF PROTEIN ENCODED BY GENE NO: 8

This gene is expressed primarily in endothelial cells, and to a lesser extent in  
30 lymph node, tonsils, heart and spinal cord.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, vascular disease such as restenosis, including disorders of the  
35 integumentary system. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells,

particularly of the vascular system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., integumentary tissue, lymph tissue and other cells and tissue of the immune system, cells and tissue of the nervous system, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for treating diseases of the vasculature including problems associated with diabetes and restenosis following angioplasty. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:18 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1408 of SEQ ID NO:18, b is an integer of 15 to 1422, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:18, and where b is greater than or equal to a + 14.

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#### FEATURES OF PROTEIN ENCODED BY GENE NO: 9

The translation product of this gene was shown to have homology to the Gcap1 gene product of *Mus musculus*, which is specifically expressed in cerebellum and appears to be developmentally regulated (See Genbank Accession No. gil862343).

This gene is expressed primarily in fetal lung and endothelial cells and to a lesser extent in astrocytes and fetal brain.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, endothelial cell proliferation as in restenosis. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes

for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the vascular system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., developmental tissue, neural tissue, and cancerous and wounded tissues) or bodily fluids (e.g., amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in fetal brain, in addition to the homology to a brain-specific regulatory protein indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states and behavioural disorders such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tumors and tissues. Alternatively, The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for treating abnormal proliferation of endothelial cells such as occurs upon injury to the lung or arteries. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:19 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1093 of SEQ ID NO:19, b is an integer of 15 to 1107, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:19, and where b is greater than or equal to a + 14.

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#### FEATURES OF PROTEIN ENCODED BY GENE NO: 10

This gene maps to chromosome 12, and therefore, may be used as a marker in linkage analysis for chromosome 12.

This gene is expressed primarily in infant brain and fetal tissues.

5 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, developmental abnormalities during gestation such as spina bifida. Similarly, polypeptides and antibodies directed to these polypeptides are useful in  
10 providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the Central nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., developing and/or differentiating cells and tissue, and nervous tissue, and cancerous and wounded tissues) or bodily fluids  
15 (e.g., amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides  
20 corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states and behavioural disorders such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered bahaviors, including disorders in feeding, sleep  
25 patterns, balance, and preception. In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tumors and tissues.  
30 Alternatively, The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of cancer and other proliferative disorders. Expression within embryonic tissue and other cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division. Similarly, embryonic development also involves  
35 decisions involving cell differentiation and/or apoptosis in pattern formation. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Many polynucleotide sequences, such as EST sequences, are

publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:20 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1169 of SEQ ID NO:20, b is an integer of 15 to 1183, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:20, and where b is greater than or equal to a + 14.

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#### FEATURES OF PROTEIN ENCODED BY GENE NO: 11

This gene is expressed primarily in fetal kidney.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, renal failure, tumors of the kidney, and/or developmental abnormalities associated with the kidney. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the renal system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., urological tissue, and cancerous and wounded tissues) or bodily fluids (e.g., amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:160 as residues: Gln-26 to Gln-34.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of cancer and other proliferative disorders, particularly renal disorders. Expression within embryonic tissue and other cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division. Similarly, embryonic development also involves decisions involving cell differentiation and/or apoptosis in pattern formation. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Many polynucleotide sequences, such as EST



sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:21 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1406 of SEQ ID NO:21, b is an integer of 15 to 1420, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:21, and where b is greater than or equal to a + 14.

#### FEATURES OF PROTEIN ENCODED BY GENE NO: 12

This gene is expressed primarily in breast, fetal kidney, and T-cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions: autoimmune disease, chronic inflammatory conditions, immune disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., immune cells and tissue, and reproductive tissue, and cancerous and wounded tissues) or bodily fluids (e.g., breast milk, lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:161 as residues: His-2 to Lys-7, Ser-28 to Glu-35.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of a variety of immune system disorders. Expression of this gene product in T-cells indicates a role in the regulation of the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer e.g., by

boosting immune responses. Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, and leukemia. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tumors and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:22 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1561 of SEQ ID NO:22, b is an integer of 15 to 1575, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:22, and where b is greater than or equal to a + 14.

### FEATURES OF PROTEIN ENCODED BY GENE NO: 13

This gene is expressed primarily in the frontal cortex of the brain. Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neurodegenerative disorders, ischemia, Alzheimer's, Parkinson's. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., neural tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue

or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:162 as residues: Glu-31 to Gly-37.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states and behavioural disorders such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tumors and tissues. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:23 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 527 of SEQ ID NO:23, b is an integer of 15 to 541, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:23, and where b is greater than or equal to a + 14.

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#### FEATURES OF PROTEIN ENCODED BY GENE NO: 14

This gene maps to chromosome 1, and therefore, may be used as a marker in linkage analysis for chromosome 1.

30 This gene is expressed primarily in ovary and to a lesser extent in infant brain.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions: cancers and other diseases of the female reproductive system including ovarian cysts and hormonal disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of

the female reproductive system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., reproductive tissue, neural cells and tissue, and cancerous and wounded tissues) or bodily fluids (e.g., amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:163 as residues: Ser-32 to Glu-37.

The tissue distribution in ovarian tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and intervention of ovarian tumors, in addition to other tumors where expression has been indicated. Protein, as well as, antibodies directed against the protein may show utility as a tissue-specific marker and/or immunotherapy target for the above listed tissues. Alternatively, expression within the fetal brain indicates that the protein product of this gene is useful for the detection/treatment of neurodegenerative disease states and behavioural disorders such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:24 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 819 of SEQ ID NO:24, b is an integer of 15 to 833, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:24, and where b is greater than or equal to a + 14.

### 35 FEATURES OF PROTEIN ENCODED BY GENE NO: 15

The translation product of this gene was shown to have homology to the highly conserved ras gene which is known to be important in the regulation of cell growth, and thus has been shown to serve as an inducible oncogene in eukaryotic tissues (See Genbank Accession No. gblZ11804|DDRASX). When tested against PC12 (rat pheochromocytoma cells) cell lines, supernatants removed from cells containing this gene activated the EGR1 (early growth response gene 1) pathway. Thus, it is likely that this gene activates sensory neuron cells through the EGR1 signal transduction pathway. The EGR1 (early growth response gene 1) is a separate signal transduction pathway from Jaks-STAT, genes containing the EGR1 promoter are induced in various tissues and cell types upon activation, leading the cells to undergo differentiation and proliferation.

This gene is expressed primarily in T-cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases involving immune regulation including autoimmune diseases such as rheumatoid arthritis, lupus, and leukemia. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., immune cells and tissue, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:164 as residues: Ala-28 to His-41, Pro-43 to Gln-64.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of a variety of immune system disorders. Expression of this gene product in T-cells indicates a role in the regulation of the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer - particularly considering the homology to a conserved ras gene, combined with the detected EGR1 biological activity. Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an

agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, and leukemia. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tumors and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:25 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1541 of SEQ ID NO:25, b is an integer of 15 to 1555, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:25, and where b is greater than or equal to a + 14.

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#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 16**

This gene maps to chromosome 13, and therefore, may be used as a marker in linkage analysis for chromosome 13.

25 This gene is expressed primarily in kidney cortex.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases of the kidney including cancer and renal dysfunction. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the renal system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., urogenital tissue, and cancerous and wounded tissues) or bodily fluids (e.g., urine, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to

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the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment/diagnosis of diseases of the kidney including kidney failure. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:26 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1529 of SEQ ID NO:26, b is an integer of 15 to 1543, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:26, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 17

This gene is expressed primarily in T-cell lymphoma and to a lesser extent in bone marrow stromal cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cancer including lymphomas and leukemias. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., immune cells and tissue, and bone marrow, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of a variety of

immune system disorders. Expression of this gene product in T-cells indicates a role in the regulation of the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g., by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, and leukemia. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tumors and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Expression in bone marrow cells suggest that the protein product of this gene is useful for the treatment and diagnosis of hematopoietic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:27 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1248 of SEQ ID NO:27, b is an integer of 15 to 1262, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:27, and where b is greater than or equal to a + 14.



## FEATURES OF PROTEIN ENCODED BY GENE NO: 18

This gene is expressed primarily in a medulloblastoma.

5        Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, disorders of the central nervous system including cancers. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing  
10 immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., neural cells and tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or  
15 another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:167 as residues: Phe-22 to Leu-28.

      The tissue distribution indicates that polynucleotides and polypeptides  
20 corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states and behavioural disorders such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep  
25 patterns, balance, and preception. In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Many  
30 polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:28 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly,  
35 preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 739 of SEQ ID NO:28, b is an integer of 15 to 753, where

both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:28, and where b is greater than or equal to a + 14.

## 5 FEATURES OF PROTEIN ENCODED BY GENE NO: 19

The translation product of this gene was shown to have homology to the mammalian notch I protein which has been shown to be important in the regulation of cell-fate during pattern formation and development (See Genbank Accession No. gil57635). One embodiment of this gene comprises polypeptides of the following amino acid sequence: KHEXHQVSDGALRCFASLADRFRRGVDPAPLAKHGLTEE  
 10 LLSRMAAAGGTVSGPSSACKPXRSTTGAPSTTADSKLSNQVSTIVSLLSTLCRG  
 SPVVTHDLLRSELPDSIESALQGDERCVLDTMRLVDFLLVLLFEGRKALPKSSA  
 GSTG RIPGLRRLDSSGERSHRQLIDCIRSKDTDALIDAIDTGAFEVN  
 15 FMDDVGQTLNWA SAFGTQEMVEFLCERGADVNRGQRSSSLHYAACF  
 GRPQVAKTLLRHGANPDLRDEDGKTPLDKARERGHSEVVAILQSPGDW  
 MCPVNKGDDK (SEQ ID NO:311), PLDKARERGHSEVVAIL (SEQ ID NO:312),  
 and/or AKTLLRHGANPDLRD (SEQ ID NO:313). Additional embodiments are directed to polynucleotides encoding these polypeptides.

20 This gene is expressed primarily in endothelial cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases involving angiogenic abnormalities including diabetic  
 25 retinopathy, macular degeneration, and other diseases including arteriosclerosis and cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the vascular system, expression of this gene at significantly higher or lower levels may be  
 30 routinely detected in certain tissues (e.g., endothelial cells, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in  
 35 epitopes include those comprising a sequence shown in SEQ ID NO:168 as residues: Asp-17 to Phe-23.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for treating diseases where an increase or decrease in angiogenesis is indicated and as a factor in the wound healing process. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Alternatively, considering the homology to the Notch I protein, this gene may show utility in the detection/treatment of neurodegenerative disease states and behavioural disorders such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:29 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1607 of SEQ ID NO:29, b is an integer of 15 to 1621, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:29, and where b is greater than or equal to a + 14.

#### FEATURES OF PROTEIN ENCODED BY GENE NO: 20

This gene is expressed primarily in meningioma tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cancers of the central nervous system and endothelium. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, ovarian cancer, as well as, other cancers of the female reproductive system, and endothelial tissue in general. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the female reproductive system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., reproductive tissue, and neural tissue, and cancerous and wounded tissues) or bodily fluids (e.g., amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:170 as residues: Leu-8 to Gln-18, Thr-26 to Lys-33, Met-39 to Cys-46, Ala-62 to Pro-69, Pro-83 to Glu-90.

The tissue distribution in ovary tissues indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and intervention of tumors within these tissues, in addition to other tumors where expression has been indicated. Protein, as well as, antibodies directed against the protein may show utility as a tissue-specific marker and/or immunotherapy target for the above listed tumors and tissues. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:31 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2081 of SEQ ID NO:31, b is an integer of 15 to 2095, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:31, and where b is greater than or equal to a + 14.

## 35 FEATURES OF PROTEIN ENCODED BY GENE NO: 22

This gene is expressed primarily in the spongy tissue from Alzheimer's brain.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, Alzheimer's disease and other neurodegenerative diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., neural tissue, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:171 as residues: Ser-31 to Ala-37, Ala-50 to Tyr-55, Phe-63 to Arg-68, His-83 to Pro-89.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states and behavioural disorders such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:32 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1824 of SEQ ID NO:32, b is an integer of 15 to 1838, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:32, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 23

5           This gene is expressed primarily in bone marrow cells.

          Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, hematological disorders. Similarly, polypeptides and antibodies directed  
10 to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the hematological and immune systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., immune cells and tissue, haematopoietic cells and tissue, and cancerous  
15 and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:172 as residues:  
20 Glu-22 to Ser-33, Leu-47 to Ser-55, Thr-87 to Arg-104.

          The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of hematopoietic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic  
25 lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem  
30 cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences  
35 are related to SEQ ID NO:33 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is

cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 768 of SEQ ID NO:33, b is an integer of 15 to 782, where both a and b correspond to the positions of nucleotide  
5 residues shown in SEQ ID NO:33, and where b is greater than or equal to a + 14.

#### FEATURES OF PROTEIN ENCODED BY GENE NO: 24

10 This gene is expressed primarily in neutrophils.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases of the immune system, including inflammatory diseases and  
15 allergies. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., immune cells and tissue, haematopoietic  
20 cells and tissue, blood cells, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a  
25 sequence shown in SEQ ID NO:173 as residues: Gln-36 to Lys-41.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of a variety of immune system disorders. Expression of this gene product in neutrophils indicates a role in the regulation of the proliferation; survival; differentiation; and/or activation of  
30 potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g., by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also  
35 used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, and leukemia. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy

targets for the above listed tumors and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:34 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1546 of SEQ ID NO:34, b is an integer of 15 to 1560, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:34, and where b is greater than or equal to a + 14.

#### FEATURES OF PROTEIN ENCODED BY GENE NO: 25

This gene is expressed primarily in neutrophils.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases of the immune system, including inflammatory diseases and allergies. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., immune cells and tissue, haematopoietic cells and tissue, blood cells, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of a variety of immune system disorders. Expression of this gene product in neutrophils indicates a



role in the regulation of the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g., by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, and leukemia. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tumors and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:35 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1078 of SEQ ID NO:35, b is an integer of 15 to 1092, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:35, and where b is greater than or equal to a + 14.

#### FEATURES OF PROTEIN ENCODED BY GENE NO: 26

This gene is expressed primarily in neutrophils.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases of the immune system, including inflammatory diseases and allergies. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may

be routinely detected in certain tissues (e.g., immune cells and tissue, haematopoietic cells and tissue, blood cells, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:175 as residues: Lys-9 to Leu-16, Ser-33 to Met-43.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of a variety of immune system disorders. Expression of this gene product in neutrophils indicates a role in the regulation of the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g., by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, and leukemia. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tumors and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:36 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1139 of SEQ ID NO:36, b is an integer of 15 to 1153, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:36, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 27

The translation product of this gene was shown to have homology to the intrinsic factor-B12 receptor precursor of *Rattus norvegicus* which is thought to be important in development (See Genbank Accession No. gil2961490 (AF022247)). One embodiment of this gene comprises polypeptides of the following amino acid sequence: DCNRDYHKAFGNLRSPGWPDPNDNDXDCXVTLTAPQNHHS GIVENAETISWR (SEQ ID NO:314), FGNLRS PGWPDNYDN (SEQ ID NO:315), and/or APQNHXLK CRNDFLEV (SEQ ID NO:316). Additional embodiments are directed to polynucleotides encoding these polypeptides.

This gene is expressed primarily in neutrophils.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases of the immune system, including inflammatory diseases and allergies. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., immune cells and tissue, haematopoietic cells and tissue, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of a variety of immune system disorders. Expression of this gene product in neutrophils indicates a role in the regulation of the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g., by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, and leukemia. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy

targets for the above listed tumors and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:37 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 971 of SEQ ID NO:37, b is an integer of 15 to 985, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:37, and where b is greater than or equal to a + 14.

#### FEATURES OF PROTEIN ENCODED BY GENE NO: 28

This gene is expressed primarily in neutrophils. Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune and/or haematological disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., immune cells and tissue, haematopoietic cells and tissue, blood cells, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:177 as residues: Pro-55 to Ser-66.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of a variety of

immune system disorders. Expression of this gene product in neutrophils indicates a role in the regulation of the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g., by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, and leukemia. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tumors and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:38 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1108 of SEQ ID NO:38, b is an integer of 15 to 1122, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:38, and where b is greater than or equal to a + 14.

#### FEATURES OF PROTEIN ENCODED BY GENE NO: 29

This gene is expressed primarily in neutrophils.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune and haematological disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene

at significantly higher or lower levels may be routinely detected in certain tissues (e.g., immune cells and tissue, blood cells, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of a variety of immune system disorders. Expression of this gene product in neutrophils indicates a role in the regulation of the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g., by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, and leukemia. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tumors and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:39 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 584 of SEQ ID NO:39, b is an integer of 15 to 598, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:39, and where b is greater than or equal to a + 14.

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#### FEATURES OF PROTEIN ENCODED BY GENE NO: 30

This gene is expressed primarily in ovarian cancer. This gene also maps to chromosome 7, and therefore can be used as a marker in linkage analysis for chromosome 7.

5 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, ovarian cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification  
10 of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., reproductive tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having  
15 such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of ovarian cancer. Many polynucleotide sequences, such as EST sequences, are publicly available and  
20 accessible through sequence databases. Some of these sequences are related to SEQ ID NO:40 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more  
25 polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1115 of SEQ ID NO:40, b is an integer of 15 to 1129, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:40, and where b is greater than or equal to a + 14.

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#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 31**

This gene is expressed primarily in ovarian cancer.

Therefore, polynucleotides and polypeptides of the invention are useful as  
35 reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, ovarian cancer. Similarly, polypeptides and antibodies directed to these

polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., reproductive tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of ovarian cancer. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:41 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1144 of SEQ ID NO:41, b is an integer of 15 to 1158, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:41, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 32

This gene is expressed primarily in ovarian tumor.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, ovarian cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., reproductive tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.



The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of ovarian cancer. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:42 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1753 of SEQ ID NO:42, b is an integer of 15 to 1767, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:42, and where b is greater than or equal to a + 14.

#### 15 FEATURES OF PROTEIN ENCODED BY GENE NO: 33

The translation product of this gene shares sequence homology with uroplakin III which is thought to be important in urothelial differentiation. (See Accession No. d10226610) Preferred polypeptide fragments comprise the amino acid sequence: ASIDTWPGRRSGGMIVITSI (SEQ ID NO:317) and/or GSPQAETRWSDPIALHQ GKSPASIDTWPGRRSGGMIVITSI (SEQ ID NO:318).

This gene is expressed primarily in ovarian tumor.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, ovarian cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., reproductive tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology to uroplakin III indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of ovarian cancer. Many polynucleotide sequences, such as EST

sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:43 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related  
 5 sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 903 of SEQ ID NO:43, b is an integer of 15 to 917, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:43, and where b is greater than or equal to a + 14.

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#### FEATURES OF PROTEIN ENCODED BY GENE NO: 34

The translation product of this gene shares sequence homology with estrogen-  
 15 responsive finger protein, which is thought to be important in uterine implantation. (See Accession No. 1088467; and J. Biol. Chem. 270 (41), 24406-24413 (1995), herein incorporated by reference in its entirety.) Preferred polypeptide fragments comprise the amino acid sequence:

VXDITFDPDTAHKYLRLQEENRKVTNTTPWEHPYPDLPSRFLH (SEQ ID  
 20 NO:319); LYLHRYFFEVEIFGAGTYV (SEQ ID NO:320); SCISGNNFSW  
 SLQWNGKEFTAW (SEQ ID NO:321); TPLKAGPFWSGSLTS (SEQ ID NO:322);  
 SVSEVKAVAEMQFGELLA AVRKAQANVMLFLXEKEQAAL (SEQ ID NO:323);  
 EKSKQELETMA AISNTVQFLECYCKFKNTEDITFPSVYIGLKD (SEQ ID  
 NO:324); LENYKKKLQEF SKEEYDIRTQVSAXVQR (SEQ ID NO:325); and/or  
 25 GVIYIDFPGGILSFYGVYDS MTLVHKFACKFSEPVYAA (SEQ ID NO:326). Also  
 preferred are polynucleotide fragments encoding these polypeptide fragments.

This gene is expressed primarily in ovarian cancer.

Therefore, polynucleotides and polypeptides of the invention are useful as  
 reagents for differential identification of the tissue(s) or cell type(s) present in a  
 30 biological sample and for diagnosis of diseases and conditions which include, but are  
 not limited to, ovarian cancer and other disorders of the reproductive system. Similarly,  
 polypeptides and antibodies directed to these polypeptides are useful in providing  
 immunological probes for differential identification of the tissue(s) or cell type(s). For a  
 number of disorders of the above tissues or cells, particularly of the reproductive  
 35 system, expression of this gene at significantly higher or lower levels may be routinely  
 detected in certain tissues (e.g., reproductive tissue, and cancerous and wounded  
 tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or

another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology to estrogen-responsive finger protein indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of ovarian cancer and other disorders of the reproductive system. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:44 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1973 of SEQ ID NO:44, b is an integer of 15 to 1987, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:44, and where b is greater than or equal to a + 14.

#### FEATURES OF PROTEIN ENCODED BY GENE NO: 35

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This gene shows sequence homology to a *Caenorhabditis elegans* gene, called D1054.3. (See Accession No. gnllPIDe348554.) Preferred polypeptide fragments comprise the amino acid sequence:

SKIKYDWYQTESQVVITLMIKNVQKNDVNVEFSEKELSALVKLPSGEDYNLKL  
 25 ELLHPIPEQSTFKVLSTKIEIKLKKPEAVRWEKLEGQGDVPTPKQFVADVKNLY  
 PSSSPYTRNWDKLVGEIKEEEKNEKLEGDAALNRLFQQIYSDGSDEVKR  
 AMNKSFMESGGTVLSTNWSVDVGKRKVEINPPDDMEWKKY (SEQ ID NO:327);  
 GDAALN RLFQQIYSDGSDEVKRAMNKSFMESGGTVLSTN (SEQ ID NO:328);  
 and/or DWYQTESQ VVITLMIKNVQKNDV (SEQ ID NO:329). Also preferred are  
 30 polynucleotide fragments encoding these polypeptide fragments.

This gene is expressed primarily in osteoclastoma.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, osteoclastoma and other forms of cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders

of the above tissues or cells, particularly of the bone system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., bone cells, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of osteoclastoma and other forms of cancers. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:45 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2039 of SEQ ID NO:45, b is an integer of 15 to 2053, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:45, and where b is greater than or equal to a + 14.

#### FEATURES OF PROTEIN ENCODED BY GENE NO: 36

This gene is expressed primarily in Human Placenta.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases of embryonic and reproductive systems. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the embryonic and reproductive systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., reproductive tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of the disorders of embryonic and reproductive systems. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:46 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1258 of SEQ ID NO:46, b is an integer of 15 to 1272, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:46, and where b is greater than or equal to a + 14.

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#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 37**

This gene is expressed primarily in Anergic T-cell.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, blood cell disorders, especially those involved with T-cells. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., cells and tissue of the immune system, blood cells, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of T cell related disorders. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:47 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded

from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 759 of SEQ ID NO:47, b is an integer of 15 to 773, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:47, and where b is greater than or equal to a + 14.

### FEATURES OF PROTEIN ENCODED BY GENE NO: 38

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The translation product of this gene shares sequence homology with a murine bone-related sulphatase. (See Accession No. 3046314.)

This gene is expressed primarily in retina.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, eye diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the eye, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., bone cells and tissue, retinal cells and other cells and tissue of the nervous system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:187 as residues: Ala-21 to Arg-27, Asp-40 to Arg-45, Glu-97 to Thr-110, Glu-117 to Lys-128, Arg-175 to Lys-182, Pro-207 to Gly-220, Val-253 to Ile-272.

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The tissue distribution and homology to sulphatases indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of eye disorders. Moreover, this gene may be involved in bone-related disorders, osteoporosis, Paget's disease, osteomalacia, and diagnosis. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:48 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the

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present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2105 of SEQ ID NO:48, b is an integer of 15 to 2119, where  
5 both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:48, and where b is greater than or equal to a + 14.

### FEATURES OF PROTEIN ENCODED BY GENE NO: 39

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This gene is expressed primarily in human stomach cancers.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are  
15 not limited to, cancer, particularly of the gastrointestinal system. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the cancer, expression of this gene at significantly higher or lower levels may be routinely detected in certain  
20 tissues (e.g., gastrointestinal tissue, endothelial cells and tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

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The tissue distribution in tumors of the stomach indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and intervention of these tumors, in addition to other tumors where expression has been indicated. Protein, as well as, antibodies directed against the protein may show utility as a tissue-specific marker and/or immunotherapy target for the above listed tissues. Many polynucleotide  
30 sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:49 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably  
35 excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1174 of SEQ ID NO:49, b is an integer of 15 to 1188, where both a and b

correspond to the positions of nucleotide residues shown in SEQ ID NO:49, and where b is greater than or equal to a + 14.

## 5 FEATURES OF PROTEIN ENCODED BY GENE NO: 40

This gene is expressed primarily in human synovial membrane.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases of synovial membrane and musculoskeletal disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the synovial membrane system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., synovial cells and tissue, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:189 as residues: Pro-10 to Ser-20.

The tissue distribution within synovial tissue indicates the product of this gene may a role in the detection and treatment of disorders and conditions affecting the skeletal system, in particular the connective tissues (e.g., arthritis, trauma, tendonitis, chondromalacia and inflammation). Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:50 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 464 of SEQ ID NO:50, b is an integer of 15 to 478, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:50, and where b is greater than or equal to a + 14.



**FEATURES OF PROTEIN ENCODED BY GENE NO: 41**

5           The translation product of this gene shares sequence homology with adipose specific collagen-like factor as well as the human adipocyte complement related protein Acrp30, the latter of which is known to be important in energy balance and homeostasis involving food intake, particularly in carbohydrate and lipid catabolism/anabolism (See Genbank Accession Nos.gnllPIDld1008822 and W09108, respectively). In specific  
 10   embodiments, polypeptides of the invention comprise the amino acid sequence:  
 XLWDPGLPGVCRCGSIVLKSAFSVGITTSYPEXRLPIIFNKVLLPRGXALQPCH  
 R GSSSVLSQGIYYFSYDITLANKHLAIGLVHNGQYRIKTFDANTGNHDTVASG  
 STVIYLQPEDEVWLEIFFTDQNGLFSDPGWADSLFSGFLLYVDTDYLDSE  
 DDEL (SEQ ID NO:330), GSIVLKSAFSVGITT (SEQ ID NO:331), GIYYFSYDITLA  
 15   NK (SEQ ID NO:332), DSLFSGFLLYVDT (SEQ ID NO:333), and/or NHDVASGST  
 VIYL (SEQ ID NO:334). Additional embodiments are directed to the polynucleotides encoding these polypeptides.

          This gene is expressed primarily in human schwannoma.

          Therefore, polynucleotides and polypeptides of the invention are useful as  
 20   reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neurofibroma, and other neural disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders  
 25   of the above tissues or cells, particularly of the diseases relating to peripheral or sympathetic nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and locations (e.g., neural cells and tissue, integumentary tissue, extracellular matrix, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another  
 30   tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:190 as residues: Gly-16 to Pro-30, Pro-42 to Gly-56, Gly-62 to Gly-77, Glu-93 to Gly-104, Glu-109 to Glu-114, Pro-121 to  
 35   Asp-126.

          The tissue distribution combined with the homology to a conserved human adipose specific collagen-like factor as well as to the human adipocyte complement

related protein Acrp30, indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states and behavioural disorders particularly neuroschwannoma, and including Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered bahaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Alternatively, considering the homology to a conserved adipose specific collagen-like factor, would suggest that this protein may also be important in the diagnosis or treatment of various autoimmune disorders such as rheumatoid arthritis, lupus, scleroderma, and dermatomyositis as well as dwarfism, spinal deformation, and specific joint abnormalities as well as chondrodysplasias ie. spondyloepiphyseal dysplasia congenita, familial osteoarthritis, Atelosteogenesis type II, metaphyseal chondrodysplasia type Schmid. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:51 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1319 of SEQ ID NO:51, b is an integer of 15 to 1333, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:51, and where b is greater than or equal to a + 14.

30

#### FEATURES OF PROTEIN ENCODED BY GENE NO: 42

This gene is expressed primarily in human activated T-Cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immunodeficiency, and other immune disorders. Similarly, polypeptides

and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the disorders of the immune system, expression of this gene at significantly higher or lower levels may be routinely  
5 detected in certain tissues (e.g., immune cells and tissue, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

10 The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of a variety of immune system disorders. Expression of this gene product in T-cells indicates a role in the regulation of the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product  
15 may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g., by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune  
20 deficiency diseases such as AIDS, and leukemia. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tumors and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types.  
25 Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:52 and may have been publicly available prior to conception of the present invention. Preferably,  
30 such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1241 of SEQ ID NO:52, b is an integer of 15 to 1255, where both a and b  
35 correspond to the positions of nucleotide residues shown in SEQ ID NO:52, and where b is greater than or equal to a + 14.

**FEATURES OF PROTEIN ENCODED BY GENE NO: 43**

5           This gene is expressed primarily in human activated T-Cells.

          Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immunodeficiencies and other immune disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the disorders of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., immune cells and tissue, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:192 as residues: Glu-15 to Arg-23, Asn-79 to Gly-84.

          The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of a variety of immune system disorders. Expression of this gene product in T-cells indicates a role in the regulation of the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g., by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, and leukemia. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tumors and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Many polynucleotide

sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:53 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1126 of SEQ ID NO:53, b is an integer of 15 to 1140, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:53, and where b is greater than or equal to a + 14.

#### FEATURES OF PROTEIN ENCODED BY GENE NO: 44

This gene is expressed primarily in human tonsil.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, inflammatory and immune diseases and/or disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune diseases, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., immune cells and tissue, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:193 as residues: Ile-2 to Lys-9, Gln-43 to Phe-49, Asn-59 to His-69, Gly-87 to Asp-93.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of a variety of immune system disorders. Expression of this gene product in tonsils indicates a role in the regulation of the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g., by

boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, and leukemia. Protein, as well as, antibodies

5 directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tumors and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor

10 marker and/or immunotherapy targets for the above listed tissues. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:54 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present

15 invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1206 of SEQ ID NO:54, b is an integer of 15 to 1220, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:54, and where

20 b is greater than or equal to a + 14.

#### FEATURES OF PROTEIN ENCODED BY GENE NO: 45

25 The translation product of this gene shares sequence homology with a novel human G52-24 secreted protein as well as the early lymphocyte activation antigen CD69, the latter of which has been shown to be important in lymphocyte proliferation and functions as a signal transmitting receptor in lymphocytes, natural killer cells, and platelets (See Genbank Accession Nos. W27288 and gil558352, respectively).

30 Preferred polypeptides comprise the following amino acid sequence:

ENFLRLRYKGPSDHWIGLSREQGQPWKWINGTEWTRQLVMKEDGANLYVAKV  
 SQVPRMNPXLS WVLLCYPGWSAVXTIVAHC SLDFPGSK (SEQ ID NO:335),  
 ELTAIK SHQYVLQAACPESWIGFQRKCFYFSDDTKNWTSSQRFCDSDADLA  
 QVESFQELVRK (SEQ ID NO:336), WIGLSREQGQPWKWING (SEQ ID NO:337),  
 35 CPESWIG FQRKC (SEQ ID NO:338), NFLRLRYKGPSDHWIGL (SEQ ID NO:339),  
 ASHLRLL SSWDYRFPILGAGECAYLNDKGASSARHYTERKWICKS KSDIHV  
 (SEQ ID NO:340), ENFLRLRYKGPSDHWIGLSREQGQPWKWINGTEWTRQL

VMKEDG ANLYVAKVSQVPRMNPXLSWVLLCYPGWSAVXTTIVAHCSLDF  
 PGSK (SEQ ID NO:341), and/or SWTSSLLNXCLHSKEHSIKATTWRLFFXILTIIL  
 CGMVAALSA IRANCHQEPSVCSSSCMPRKLDWFSKKVFLFF (SEQ ID  
 NO:342). Also preferred are the polynucleotides encoding these polypeptides.

5 This gene is expressed primarily in human testis.

Therefore, polynucleotides and polypeptides of the invention are useful as  
 reagents for differential identification of the tissue(s) or cell type(s) present in a  
 biological sample and for diagnosis of diseases and conditions which include, but are  
 not limited to, relating to male reproductive endocrine and immune disorders. Similarly,  
 10 polypeptides and antibodies directed to these polypeptides are useful in providing  
 immunological probes for differential identification of the tissue(s) or cell type(s). For a  
 number of disorders of the above tissues or cells, particularly of the disorders of  
 reproductive system, expression of this gene at significantly higher or lower levels may  
 be routinely detected in certain tissues (e.g., immune cells and tissue, reproductive  
 15 tissue, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, seminal  
 fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell  
 sample taken from an individual having such a disorder, relative to the standard gene  
 expression level, i.e., the expression level in healthy tissue or bodily fluid from an  
 individual not having the disorder. Preferred epitopes include those comprising a  
 20 sequence shown in SEQ ID NO:194 as residues: Asn-20 to Pro-25, Ser-48 to Asp-65.

The tissue distribution indicates that polynucleotides and polypeptides  
 corresponding to this gene are useful for the diagnosis and treatment of a variety of  
 immune system disorders. Homology of this gene product to the early lymphocyte  
 activation antigen CD69 indicates a role in the regulation of the proliferation; survival;  
 25 differentiation; and/or activation of potentially all hematopoietic cell lineages, including  
 blood stem cells. This gene product may be involved in the regulation of cytokine  
 production, antigen presentation, or other processes that may also suggest a usefulness  
 in the treatment of cancer (e.g., by boosting immune responses). Since the gene is  
 expressed in cells of lymphoid origin, the natural gene product may be involved in  
 30 immune functions. Therefore it may be also used as an agent for immunological  
 disorders including arthritis, asthma, immune deficiency diseases such as AIDS, and  
 leukemia. Protein, as well as, antibodies directed against the protein may show utility as  
 a tumor marker and/or immunotherapy targets for the above listed tumors and tissues.  
 In addition, this gene product may have commercial utility in the expansion of stem  
 35 cells and committed progenitors of various blood lineages, and in the differentiation  
 and/or proliferation of various cell types. Protein, as well as, antibodies directed against  
 the protein may show utility as a tumor marker and/or immunotherapy targets for the

above listed tissues. Alternatively, the tissue distribution within human testis may be indicative of a role for this gene product in normal testicular function, and may implicate this gene product in male fertility, and could even suggest a use as a male contraceptive. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:55 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 680 of SEQ ID NO:55, b is an integer of 15 to 694, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:55, and where b is greater than or equal to a + 14.

15

#### FEATURES OF PROTEIN ENCODED BY GENE NO: 46

This gene is expressed primarily in human testes.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, male reproductive and endocrine disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., endocrine tissue, reproductive tissue, and cancerous and wounded tissues) or bodily fluids (e.g. seminal fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:195 as residues: Pro-20 to Trp-25, Arg-33 to Thr-38, Asn-51 to Ile-56, Gly-82 to Ser-91, Lys-151 to Arg-156.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection, treatment, and/or prevention of various endocrine disorders and cancers, particularly Addison's disease, Cushing's Syndrome, and disorders and/or cancers of the pancreas (e.g., diabetes mellitus),



adrenal cortex, ovaries, pituitary (e.g., hyper-, hypopituitarism), thyroid (e.g., hyper-, hypothyroidism), parathyroid (e.g., hyper-, hypoparathyroidism), hypothalamus, and testes. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Alternatively, expression within the human testis may be indicative of a role for this gene product in normal testicular function, and may implicate this gene product in male fertility, and could even suggest a use as a male contraceptive. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:56 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 974 of SEQ ID NO:56, b is an integer of 15 to 988, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:56, and where b is greater than or equal to a + 14.

20

#### FEATURES OF PROTEIN ENCODED BY GENE NO: 47

One embodiment of this gene comprises polypeptides of the following amino acid sequence:

25 LKGREAGAGPGTAGAPGREDANGXXRGRGGXHQLYLWVDNIPLSRPKRNLS  
RDFSDGVLVAEVIKFYFPKMVEMHNYVGTSSLQQLSNWGHILNRKVLKRLN  
FSVPDDV (SEQ ID NO:343). An additional embodiment is the polynucleotides encoding these polypeptides.

This gene is expressed primarily in human adult testis.

30 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, relating to male reproductive and endocrine disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the disorders of the reproductive system, expression of this gene at significantly higher or lower levels may

be routinely detected in certain tissues (e.g., reproductive tissue, and endocrine, cancerous and wounded tissues) or bodily fluids (e.g., seminal fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample or another tissue or cell sample taken from an individual having such a disorder, relative to the standard  
 5 gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:196 as residues: Gln-21 to Gly-33, Gln-55 to Glu-60.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the reproductive system, and may be indicative  
 10 of a role for this gene product in normal testicular function, male fertility, and/or as a male contraceptive. Protein, as well as, antibodies directed against the protein may show utility as a tissue-specific marker and/or immunotherapy target for the above listed tissues. . Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are  
 15 related to SEQ ID NO:57 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of  
 20 a-b, where a is any integer between 1 to 1486 of SEQ ID NO:57, b is an integer of 15 to 1500, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:57, and where b is greater than or equal to a + 14.

## 25 FEATURES OF PROTEIN ENCODED BY GENE NO: 48

The translation product of this gene shares sequence homology with the human M phase phosphoprotein 10 as well as ORF YJR002w of *Saccharomyces cerevisiae* (See Genbank Accession No.gnllPIDle266673). Preferred polypeptides comprise the  
 30 following amino acid sequence:

AKNSQKEENPEHVEIQKMMDSLFLKLDALSNFHFIPKPPVPEIKVVSNLPAITM  
 EE VAPVSVSDAALLAPEEIKEKNKAGDIKTA AEKTATDKKRERRKKKYQK  
 RMKIKEKEKRRKLLEKSSVDQAGKYSKTVASEKLKQLTKTGKASFIKVRTRE  
 RKLLKGTFVGEVDSKCWVTGMSEPADSPPVG (SEQ ID NO:344), LQDEGKD  
 35 KALKSSQAFFSKLQDQVKMQINDAKKTEKKKKRQDISVHKLKL (SEQ ID  
 NO:345), DEGK DKALKSSQAFFSKLQDQVKMQINDA (SEQ ID NO:346),  
 EENPEHVEIQKMMDSLFL KLDALSNFHF (SEQ ID NO:347), SSVDQAGKYSK

TVASEKLKQLTKTGKASFIK (SEQ ID NO:349), VSVSDAALLAPEEIKEK NKAGDI (SEQ ID NO:350), and/or SNLPAITMEEVAP (SEQ ID NO:348). Also preferred are the polynucleotides encoding these polypeptides.

This gene is expressed primarily in human thyroid.

5 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases relating to the thyroid gland, particularly hyper- and hypothyroidism. Similarly, polypeptides and antibodies directed to these polypeptides  
10 are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the disorders of the endocrine system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., endocrine tissue, and cancerous and wounded tissues) or bodily fluids (e.g., lymph,  
15 serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides  
20 corresponding to this gene are useful for metabolic disorders, particularly hyper-, hypothyroidism, Graves' disease Hashimoto's thyroiditis, and/or cancer or neoplasias of the thyroid, and/or other endocrine organs and immune system. Protein, as well as, antibodies directed against the protein may show utility as a tissue-specific marker and/or immunotherapy target for the above listed tissues. Many polynucleotide  
25 sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:58 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably  
30 excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1377 of SEQ ID NO:58, b is an integer of 15 to 1391, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:58, and where b is greater than or equal to a + 14.

In the present invention, a "polynucleotide fragment" refers to a short polynucleotide having a nucleic acid sequence contained in the deposited clone or shown in SEQ ID NO:X. The short nucleotide fragments are preferably at least about 15 nt, and more preferably at least about 20 nt, still more preferably at least about 30 nt, and even more preferably, at least about 40 nt in length. A fragment "at least 20 nt in length," for example, is intended to include 20 or more contiguous bases from the cDNA sequence contained in the deposited clone or the nucleotide sequence shown in SEQ ID NO:X. These nucleotide fragments are useful as diagnostic probes and primers as discussed herein. Of course, larger fragments (e.g., 50, 150, 500, 600, 2000 nucleotides) are preferred.

Moreover, representative examples of polynucleotide fragments of the invention, include, for example, fragments having a sequence from about nucleotide number 1-50, 51-100, 101-150, 151-200, 201-250, 251-300, 301-350, 351-400, 401-450, 451-500, 501-550, 551-600, 651-700, 701-750, 751-800, 800-850, 851-900, 901-950, 951-1000, 1001-1050, 1051-1100, 1101-1150, 1151-1200, 1201-1250, 1251-1300, 1301-1350, 1351-1400, 1401-1450, 1451-1500, 1501-1550, 1551-1600, 1601-1650, 1651-1700, 1701-1750, 1751-1800, 1801-1850, 1851-1900, 1901-1950, 1951-2000, or 2001 to the end of SEQ ID NO:X or the cDNA contained in the deposited clone. In this context "about" includes the particularly recited ranges, larger or smaller by several (5, 4, 3, 2, or 1) nucleotides, at either terminus or at both termini. Preferably, these fragments encode a polypeptide which has biological activity. More preferably, these polynucleotides can be used as probes or primers as discussed herein.

In the present invention, a "polypeptide fragment" refers to a short amino acid sequence contained in SEQ ID NO:Y or encoded by the cDNA contained in the deposited clone. Protein fragments may be "free-standing," or comprised within a larger polypeptide of which the fragment forms a part or region, most preferably as a single continuous region. Representative examples of polypeptide fragments of the invention, include, for example, fragments from about amino acid number 1-20, 21-40, 41-60, 61-80, 81-100, 102-120, 121-140, 141-160, or 161 to the end of the coding region. Moreover, polypeptide fragments can be about 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, 120, 130, 140, or 150 amino acids in length. In this context "about" includes the particularly recited ranges, larger or smaller by several (5, 4, 3, 2, or 1) amino acids, at either extreme or at both extremes.

Preferred polypeptide fragments include the secreted protein as well as the mature form. Further preferred polypeptide fragments include the secreted protein or the mature form having a continuous series of deleted residues from the amino or the carboxy terminus, or both. For example, any number of amino acids, ranging from 1-

may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. . Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ  
5 ID NO:59 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of  
10 a-b, where a is any integer between 1 to 1565 of SEQ ID NO:59, b is an integer of 15 to 1579, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:59, and where b is greater than or equal to a + 14.

## 15 FEATURES OF PROTEIN ENCODED BY GENE NO: 50

The translation product of this gene was shown to have homology to the chicken LRP/alpha-2-macroglobulin receptor which is thought to play a pivotal role on the metabolism of alpha-2-macroglobulins, as well as, complexes between plasminogen  
20 activators and their endogenous inhibitors (See GenbankAccession No gb|X74904|GGLRPA2MR).

This gene is expressed primarily in neuronal tissues and to a lesser extent in uterine cancer.

Therefore, polynucleotides and polypeptides of the invention are useful as  
25 reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neuronal disorders and uterine cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders  
30 of the above tissues or cells, particularly of the central neuron system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., neural cells and tissue, reproductive tissue, and cancerous and wounded tissues) or bodily fluids (e.g., amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample or another tissue or cell sample taken from  
35 an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states and behavioural disorders such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered bahaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:60 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1227 of SEQ ID NO:60, b is an integer of 15 to 1241, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:60, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 51

This gene is expressed primarily in uterine cancer and to a lesser extent in other tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, uterine cancer, and other reproductive disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the uterine cancer, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., reproductive tissue, and cancerous and wounded tissues) or bodily fluids (e.g., amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another

tissue or cell sample or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

5 The tissue distribution in tumors of the uterus indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and intervention of these tumors, in addition to other tumors where expression has been indicated. Protein, as well as, antibodies directed against the protein may show utility as a tissue-specific marker and/or immunotherapy target for the above listed tissues. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through  
10 sequence databases. Some of these sequences are related to SEQ ID NO:61 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a  
15 nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 916 of SEQ ID NO:61, b is an integer of 15 to 930, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:61, and where b is greater than or equal to a + 14.

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#### FEATURES OF PROTEIN ENCODED BY GENE NO: 52

This gene is expressed primarily in Wilm's tumor and to a lesser extent in other tissues.

25 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, Wilm's tumor, and other urogenital disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological  
30 probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the Wilm's tumor, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., urogenital tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell  
35 sample or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of Wilm's tumor. Protein, as well as, antibodies directed against the protein may show utility as a tissue-specific marker and/or immunotherapy target for the above listed tissues. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:62 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 984 of SEQ ID NO:62, b is an integer of 15 to 998, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:62, and where b is greater than or equal to a + 14.

#### FEATURES OF PROTEIN ENCODED BY GENE NO: 53

The translation product of this gene was shown to have homology to the MEK kinase 3 of *Mus musculus*, mutations of which and/or aberrant regulation of, may provide a predisposition to cancer. This gene maps to chromosome 17, and therefore, may be used as a marker in linkage analysis for chromosome 17.

This gene is expressed primarily in pituitary and to a lesser extent in ulcerative colitis, hemapoietic cells, and some other tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune, gastrointestinal, haematopoeitic diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the neuronal and immune tissues, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., immune cells and tissue, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression



level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of a variety of immune system disorders. Expression of this gene product in ulcerative colitis indicates a role in the regulation of the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g., by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, and leukemia. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tumors and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:63 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1179 of SEQ ID NO:63, b is an integer of 15 to 1193, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:63, and where b is greater than or equal to a + 14.

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#### FEATURES OF PROTEIN ENCODED BY GENE NO: 54

When tested against Jurkat T-cell cell lines, supernatants removed from cells containing this gene activated the GAS (gamma activation site) pathway. Thus, it is likely that this gene activates T-cells through the Jaks-STAT signal transduction pathway. GAS (gamma activation site) is a promoter element found upstream in many

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genes which are involved in the Jaks-STAT pathway. The Jaks-STAT pathway is a large, signal transduction pathway involved in the differentiation and proliferation of cells. Therefore, activation of the Jaks-STATs pathway, reflected by the binding of the GAS element, can be used to indicate proteins involved in the proliferation and  
5 differentiation of cells.

This gene is expressed primarily in fetal spleen, adipose, and to a lesser extent in other tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a  
10 biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune, metabolic, and developmental disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the fetal spleen and  
15 adipose tissues, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., immune cells and tissue, developing cells and tissue, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample or another tissue or cell sample taken from an individual having such a disorder, relative to  
20 the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:203 as residues: Tyr-41 to Phe-47.

The tissue distribution combined with the detection of GAS promoter activation activity indicates that polynucleotides and polypeptides corresponding to this gene are  
25 useful for the diagnosis and treatment of a variety of immune system disorders. Expression of this gene product in fetal spleen indicates a role in the regulation of the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may  
30 also suggest a usefulness in the treatment of cancer (e.g., by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, and leukemia. Protein, as well as, antibodies directed against  
35 the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tumors and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood

lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through  
5 sequence databases. Some of these sequences are related to SEQ ID NO:64 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a  
10 nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 816 of SEQ ID NO:64, b is an integer of 15 to 830, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:64, and where b is greater than or equal to a + 14.

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#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 55**

This gene is expressed primarily in IL-1/TNF stimulated synovial and human adipose.

20 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, rheumatoid arthritis or obesity. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for  
25 differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., synovial and adipose cells and tissues, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or  
30 another tissue or cell sample or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:204 as residues: Leu-37 to Arg-45, Ser-60 to Ser-65.

35 The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis or treatment of rheumatoid arthritis or other immune diseases. Many polynucleotide sequences, such as EST

sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:65 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 853 of SEQ ID NO:65, b is an integer of 15 to 867, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:65, and where b is greater than or equal to a + 14.

#### FEATURES OF PROTEIN ENCODED BY GENE NO: 56

This gene is expressed primarily in aortic endothelium and to a lesser extent in melanocytes.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cardiovascular diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the cardiovascular system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., cardiovascular tissue, and melanocytes, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:205 as residues: Met-1 to Trp-12, Arg-33 to Ser-53.

The tissue distribution in human aortic endothelial cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection or intervention of cardiovascular diseases, such as hypertension, cardiovascular injuries, congenital heart diseases, ischemic heart diseases, rheumatic and other hypersensitivity diseases, cardiomyopathy. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:66 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are

specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 671 of SEQ ID NO:66, b is  
5 an integer of 15 to 685, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:66, and where b is greater than or equal to a + 14.

#### FEATURES OF PROTEIN ENCODED BY GENE NO: 57

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The translation product of this gene shares sequence homology with prostaglandin EP3-9 receptor which is thought to be important in prostaglandin hormonal reaction. In specific embodiments, polypeptides of the invention comprise the sequence:MAIPAFSSCQQISSAAALQI (SEQ ID NO:351), and/or  
15 CNGPFKHFSFTVST (SEQ ID NO:352). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in human retina.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a  
20 biological sample and for diagnosis of diseases and conditions which include, but are not limited to, glaucoma or other ocular diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the ocular system, expression of this gene at  
25 significantly higher or lower levels may be routinely detected in certain tissues (e.g., retinal and other optic tissue cells, and tissue of the nervous system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue  
30 or bodily fluid from an individual not having the disorder.

The tissue distribution in eyes and homology to prostaglandin receptor indicates that polynucleotides and polypeptides corresponding to this gene are useful for detection and intervention of ocular diseases like glaucoma. Specifically the receptor can be used for the identification of agonists or antagonists, anti-inflammatories for the  
35 eyes, and vasoconstrictive agents, etc. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:67 and may have been publicly available

prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the  
5 general formula of a-b, where a is any integer between 1 to 787 of SEQ ID NO:67, b is an integer of 15 to 801, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:67, and where b is greater than or equal to a + 14.

## 10 FEATURES OF PROTEIN ENCODED BY GENE NO: 58

The translation product of this gene shares weak sequence homology with *Hemophilus influenzae* outer protein P6 which is thought to be important in host cell interaction.

15 This gene is expressed primarily in human adrenal gland tumor.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, adrenal insufficiency or hyperfunction. Similarly, polypeptides and  
20 antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the endocrine systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., adrenal gland, and cancerous and wounded tissues) or bodily fluids (e.g., serum,  
25 plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in adrenal gland tumor and homology to *Hemophilus*  
30 *influenzae* outer membrane protein suggest that polynucleotides and polypeptides corresponding to this gene are useful in treating adrenal insufficiencies or hyperfunction because a secretory protein from an endocrine organ may function as a hormone. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:68 and  
35 may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly,

preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 894 of SEQ ID NO:68, b is an integer of 15 to 908, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID  
5 NO:68, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 59

10 When tested against a Jurkat T-cell line, supernatants removed from cells containing this gene activated the GAS (gamma activation site) pathway. Thus, it is likely that this gene activates T-cells through the Jaks-STAT signal transduction pathway. The GAS is a promoter element found upstream in many genes which are involved in the Jaks-STAT pathway. The Jaks-STAT pathway is a complex, signal  
15 transduction pathway involved in the differentiation and proliferation of cells. Therefore, activation of the Jaks-STATs pathway, reflected by the binding of the GAS element, can be used to indicate proteins involved in the proliferation and differentiation of cells.

20 This gene is expressed primarily in human kidney pyramid and to a lesser extent in human brain.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, nephrotic, nephritic syndromes, renal failure, hypertensive  
25 nephrosclerosis. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the renal system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., hepatic tissue, brain and other  
30 tissue of the nervous system, T-cells and other cells and tissue of the immune system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the  
35 disorder.

The tissue distribution in kidney indicates that polynucleotides and polypeptides corresponding to this gene are useful for renal diseases, including nephrotic, nephritic

syndromes, renal failure, hypertensive nephrosclerosis. Additionally, the gene product may have endocrine functions related to renal function, metabolism and homeostasis. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:69 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 682 of SEQ ID NO:69, b is an integer of 15 to 696, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:69, and where b is greater than or equal to a + 14.

## 15 FEATURES OF PROTEIN ENCODED BY GENE NO: 60

This gene is expressed primarily in both normal or cancerous human breast tissue.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, Non-neoplastic breast diseases or breast cancers. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the breast, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., mammary tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:209 as residues: Pro-20 to Ser-28.

The tissue distribution in breast indicates that polynucleotides and polypeptides corresponding to this gene are useful for either non-neoplastic breast diseases, such as congenital anomalies, gynecomastia, mastitis and abscess, duct ectasia and fat necrosis, or neoplasia in the breast. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of



these sequences are related to SEQ ID NO:70 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention

5 are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 441 of SEQ ID NO:70, b is an integer of 15 to 455, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:70, and where b is greater than or equal to a + 14.

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### FEATURES OF PROTEIN ENCODED BY GENE NO: 61

When tested against a K562 kidney cell line, supernatants removed from cells containing this gene activated the ISRE (interferon-sensitive responsive element)

15 pathway. Thus, it is likely that this gene activates kidney cells through the Jaks-STAT signal transduction pathway. The ISRE is a promoter element found upstream in many genes which are involved in the Jaks-STAT pathway. The Jaks-STAT pathway is a complex, signal transduction pathway involved in the differentiation and proliferation of cells. Therefore, activation of the Jaks-STATs pathway, reflected by the binding of the

20 ISRE element, can be used to indicate proteins involved in the proliferation and differentiation of cells. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in activated T-cells and osteoarthritis, and to a lesser extent in aortic endothelium, placenta and number of tissues or cell lines.

25 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, inflammatory conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential

30 identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., T-cells and other cells and tissue of the immune system, bone tissue, endothelium and placenta, and cancerous and wounded tissues) or bodily fluids (e.g.,

35 serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an

individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:210 as residues: Gln-36 to Glu-49, Glu-51 to Leu-66, Asp-68 to Ser-73.

5 The tissue distribution in activated T-cells and under inflammatory conditions like osteoarthritis suggest that the protein product of this gene is involved in the inflammatory reactions. Therefore it may be useful in the diagnosis or intervention in the inflammatory diseases with the involvement of T-cells, including osteoarthritis. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID  
10 NO:71 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of  
15 a-b, where a is any integer between 1 to 399 of SEQ ID NO:71, b is an integer of 15 to 413, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:71, and where b is greater than or equal to a + 14.

## 20 FEATURES OF PROTEIN ENCODED BY GENE NO: 62

This gene is expressed primarily in breast lymphnodes, B-cell lymphoma and to a lesser extent in neutrophils and bone marrow cells.

Therefore, polynucleotides and polypeptides of the invention are useful as  
25 reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, inflammation, immunodeficiency, allergy. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders  
30 of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., blood cells, hematopoietic cells, and cells and tissue of the immune system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an  
35 individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in the cells of immunological functions indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis or intervention of immunologically mediated disorders, such as allergy, immunodeficiency, immune surveillance, etc. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:72 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 835 of SEQ ID NO:72, b is an integer of 15 to 849, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:72, and where b is greater than or equal to a + 14.

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#### FEATURES OF PROTEIN ENCODED BY GENE NO: 63

The translation product of this gene shares weak sequence homology with Interferon induced 1-8 gene encoded polypeptide which is thought to be important in retroviral REV responsive element binding and thus viral replication.

This gene is expressed primarily in B-cell lymphoma.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune response to viral infections and other immunologically related disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., B-cells and other cells and tissue of the immune system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:212 as residues: Pro-47 to Asn-53.

The tissue distribution in B-cell lymphoma and homology to interferon induced 1-8 gene indicates that polynucleotides and polypeptides corresponding to this gene are useful for intervention of viral infection and other immunologically related disorders. The homology with interferon induced 1-8 REV response element binding gene  
5 indicates the gene product may bind to viral components to interfere with the entry, packaging, replication, or induce the host cell anti-viral response by interferon mediated pathways. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:73 and may have been publicly available prior to conception  
10 of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 491 of SEQ ID NO:73, b is an  
15 integer of 15 to 505, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:73, and where b is greater than or equal to a + 14.

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 64**

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This gene is expressed primarily in bone marrow.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are  
25 not limited to, hemapoiesis disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the hemapoietic system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g.,  
30 bone marrow, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in  
35 SEQ ID NO:213 as residues: Thr-45 to Tyr-50.

The tissue distribution in bone marrow indicates that polynucleotides and polypeptides corresponding to this gene are useful for hemapoiesis disorders. The gene

product may function as a growth factor or mobilization agent for the cells of myeloid or lymphoid lineages. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:74 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 705 of SEQ ID NO:74, b is an integer of 15 to 719, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:74, and where b is greater than or equal to a + 14.

#### FEATURES OF PROTEIN ENCODED BY GENE NO: 65

The translation product of this gene shares sequence homology with the familial adenomatous polyposis gene which is thought to be important in tumorigenesis of colon cancer (see, e.g., Fulton, Nature 368, 32-38 (1994); accession no. U28412; Joslyn et al., Cell 66 (3), 601-613 (1991); accession no. M73547; and Spirio et al., Nucleic Acids Res. 19 (22), 6348 (1991)). In specific embodiments, polypeptides of the invention comprise the sequence: CRWRPESAAPC (SEQ ID NO:353), TRPGRGAQAPVK (SEQ ID NO:354), MVSWMISRAVVLVFGMLYPAY (SEQ ID NO:355), GMLYPAYYSYKAVKTKN (SEQ ID NO:356), EYVRWMMYWIVFALYTV (SEQ ID NO:357), YPAYYSYKAVKTKNVKE (SEQ ID NO:358), VAWFPLYELKIA (SEQ ID NO:359), and/or MVSWMISRAVVLVFGMLYPAYYSYKAVKTKNVKEYVRWMMYWIVFALYTVIETVADQTVAWFPLYELKIAFVIWLLSPYTKGASLIYRKFLHPLLSSKEREIDDYIVQAKERGYETMVNFRQGLNL AATAAVTAAVKSQGAITERLRSFSMHDLTITQGDPEVQRPYQLPEAKKKXSXQPPVN (SEQ ID NO:360). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in osteoclastoma, prostate, bone marrow and to a lesser extent in testes and dendritic cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, colon cancer and cancers of various origin, including osteoclastoma and prostate cancer. Similarly, polypeptides and antibodies directed to these polypeptides

are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the tumorigenesis, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., bone, prostate, bone marrow, colon and other gastrointestinal tissue, tissue of the nervous system, and testis and other reproductive tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:214 as residues: Ser-59 to Ile-64, Ala-71 to Tyr-76, Pro-125 to Ser-141.

The tissue distribution in osteoclastoma, prostate, bone marrow and homology to familial adenomatous polyposis gene indicates polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and intervention of tumors of various origins, including colon cancer, osteoclastoma and prostate cancer. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:75 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1260 of SEQ ID NO:75, b is an integer of 15 to 1274, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:75, and where b is greater than or equal to a + 14.

#### FEATURES OF PROTEIN ENCODED BY GENE NO: 66

The translation product of this gene shares regional and weak sequence homology with neu differentiation factor and a serine protease N-terminal fragment which contains a EGF-like domain and is thought to be important in growth and differentiation of several cell types, including colon epithelial cells and Schwann cells. This gene is expressed primarily in fetal lung, bone marrow, fetal liver and to a lesser extent in brain.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, tissue injuries or diseases in lung, bone marrow, or liver. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the liver and lung, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., lung and pulmonary tissue, bone marrow, hepatic tissue, neural tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology to neu differentiation factor indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis or intervention of liver or lung injuries, including hepatic failure, recovery from hepatitis, cirrhosis, and complication from liver transplantation. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:76 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 505 of SEQ ID NO:76, b is an integer of 15 to 519, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:76, and where b is greater than or equal to a + 14.

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#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 67**

This gene is expressed primarily in activated T-cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, arthritis, asthma, auto-immune and immunodeficiency diseases.

Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., T-cells and other cells and tissue of the immune system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The expression of this gene in T-cells indicates a potential role in the treatment/detection of immune disorders such as such as arthritis, asthma, for hypersensitivity reactions and transplant rejection, and also in immune deficiency diseases such as AIDS, and leukemia. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:77 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 375 of SEQ ID NO:77, b is an integer of 15 to 389, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:77, and where b is greater than or equal to a + 14.

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#### FEATURES OF PROTEIN ENCODED BY GENE NO: 68

This gene maps to chromosome 7, accordingly, polynucleotides of the invention may be used in linkage analysis as a marker for chromosome 7.

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This gene is expressed primarily in brain and to a lesser extent in breast.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neurodegenerative conditions and behavioural disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous

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system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., brain and other tissue of the nervous system, mammary tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample  
5 taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:217 as residues: Leu-40 to His-46.

The tissue distribution indicates that polynucleotides and polypeptides  
10 corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states and behavioural disorders such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder and panic disorder. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of  
15 these sequences are related to SEQ ID NO:78 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the  
20 general formula of a-b, where a is any integer between 1 to 809 of SEQ ID NO:78, b is an integer of 15 to 823, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:78, and where b is greater than or equal to a + 14.

## 25 **FEATURES OF PROTEIN ENCODED BY GENE NO: 69**

The translation product of this gene shares sequence homology with a rat secretory carrier membrane protein which is believed to play a role in cell surface recycling. See e.g., Brand et al., EMBO J, 1993, Oct;12(10):3753-3761. Secretory  
30 carrier membrane proteins (SCAMPs) are widely distributed as components of post-Golgi membranes that function as recycling carriers to the cell surface. In fibroblasts, SCAMPs are concentrated in compartments involved in the endocytosis and recycling of cell surface receptors while in neurons and other cell types having regulated transport pathways, SCAMPs are also components of regulated carriers (synaptic vesicles,  
35 secretion granules and transporter vesicles). Their presence in multiple pathways distinguishes them from proteins (e.g., recycling cell surface receptors and synaptic vesicle proteins) which are concentrated in selected pathways. The SCAMPs also do

not appear to reside beyond the boundaries of these pathways. This distribution indicates that SCAMPs are general markers of membranes that function in cell surface recycling. Accordingly, polypeptides of the invention and antibodies thereto, may be used to identify membranes that function in cell surface recycling.

5           This gene is expressed primarily in hematopoietic cell types.

          Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune and hematopoietic disorders. Similarly, polypeptides and  
10   antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and hematopoietic systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., hematopoietic cells, and cancerous and wounded  
15   tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:218 as residues: Ser-25 to Gly-31, Gln-  
20   149 to Ser-155.

          The hematopoietic tissue distribution and homology to a cell surface molecule indicates polynucleotides and polypeptides corresponding to this gene are useful for the detection and/or treatment of immune or hematopoietic disorders including arthritis, asthma and immunodeficiency diseases. Many polynucleotide sequences, such as EST  
25   sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:79 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention  
30   are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2441 of SEQ ID NO:79, b is an integer of 15 to 2455, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:79, and where b is greater than or equal to a + 14.

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**FEATURES OF PROTEIN ENCODED BY GENE NO: 70**

This gene maps to chromosome 4. Accordingly, polynucleotides of the invention may be used in linkage analysis as a marker for chromosome 4. When tested  
5 against a Jurkat T-cell line, supernatants removed from cells containing this gene activated the GAS (gamma activation site) pathway. Thus, it is likely that this gene activates T-cells through the Jaks-STAT signal transduction pathway. The GAS is a promoter element found upstream in many genes which are involved in the Jaks-STAT pathway. The Jaks-STAT pathway is a complex, signal transduction pathway involved  
10 in the differentiation and proliferation of cells. Therefore, activation of the Jaks-STATs pathway, reflected by the binding of the GAS element, can be used to indicate proteins involved in the proliferation and differentiation of cells.

This gene is expressed primarily in brain.

Therefore, polynucleotides and polypeptides of the invention are useful as  
15 reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neurodegenerative conditions and behavioural disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a  
20 number of disorders of the above tissues or cells, particularly of the brain and central nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., brain and other tissue of the nervous system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken  
25 from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:219 as residues: Asp-57 to Gly-64.

The tissue distribution of this gene primarily in brain indicates that  
30 polynucleotides and polypeptides corresponding to this gene are useful for the treatment and/or detection of neurodegenerative disease states and behavioural disorders such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder and panic disorder. Many polynucleotide sequences, such as EST sequences, are publicly  
35 available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:80 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded

from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 907 of SEQ ID NO:80, b is an integer of 15 to 921, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:80, and where b is greater than or equal to a + 14.

#### FEATURES OF PROTEIN ENCODED BY GENE NO: 71

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This gene is expressed primarily in hematopoietic cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, autoimmune and immunodeficiency disease states. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the hematopoietic system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., hematopoietic cells, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution of this gene predominantly in hematopoietic cell types indicates that polynucleotides and polypeptides corresponding to this gene are important for the treatment or detection of immune or hematopoietic disorders including arthritis, asthma, immunodeficiency diseases, leukemia, hypersensitivity and transplant rejection. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:81 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 664 of SEQ ID NO:81, b is an integer of 15 to

678, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:81, and where b is greater than or equal to a + 14.

## 5 FEATURES OF PROTEIN ENCODED BY GENE NO: 72

This gene is expressed primarily in hematopoietic cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, auto-immune and immunodeficiency disease states. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the hematopoietic system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., hematopoietic cells, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution of this gene predominantly in hematopoietic cell types indicates that polynucleotides and polypeptides corresponding to this gene are important for the treatment or detection of immune or hematopoietic disorders including arthritis, asthma, immunodeficiency diseases, leukemia, and transplant rejection. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:82 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 843 of SEQ ID NO:82, b is an integer of 15 to 857, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:82, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 73

The translation product of this gene shares sequence homology with rat synaptogyrin which is thought to be important in membrane trafficking (see e.g.,  
 5 Stenius et al., J. Cell Biol. 131 (6 Pt 2), 1801-1809 (1995)). In specific embodiments, polypeptides of the invention comprise the sequence: QPYQVLPSRQVFALI (SEQ ID NO:361), VFSCI YGEGYSNAHESKQMYCVFN (SEQ ID NO:362), RNEDACRYGSAIGVLAFL (SEQ ID NO:363), LVVDAYFPQISNATDRK (SEQ ID NO:364), and/or SALWTFLWFGFC FLTNQWAVTNPK (SEQ ID NO:365).

10 Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in breast and ovary and to a lesser extent in most hematopoietic tissue types.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a  
 15 biological sample and for diagnosis of diseases and conditions which include, but are not limited to, female infertility and female reproductive abnormalities. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive  
 20 system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., mammary tissue, and ovary and other reproductive tissue, haematopoietic cells and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene  
 25 expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:222 as residues: Pro-9 to Trp-18, Thr-20 to Ala-27.

The tissue distribution in ovary and breast and homology to a protein involved in membrane trafficking indicates that polynucleotides and polypeptides corresponding  
 30 to this gene play a role in the detection/treatment of female fertility disorders, endocrine disorders, ovarian failure, amenorrhea, ovarian cancer, and also potentially in both non-neoplastic breast diseases such as congenital abnormalities and neoplasia in the breast.. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID  
 35 NO:83 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.

Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1963 of SEQ ID NO:83, b is an integer of 15 to 1977, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:83, and where b is greater than or equal to a + 14.

#### FEATURES OF PROTEIN ENCODED BY GENE NO: 74

10           This gene maps to chromosome 12, and therefore polynucleotides of the invention may be used in linkage analysis as a marker for chromosome 12.

          This gene is expressed primarily in brain and to a lesser extent in placenta and spleen.

          Therefore, polynucleotides and polypeptides of the invention are useful as  
15   reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, behavioural disorders and neurodegenerative disease states. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a  
20   number of disorders of the above tissues or cells, particularly of the brain and central nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., brain and other tissue of the nervous system, spleen and other cells and tissue of the immune system, placenta, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal  
25   fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

          The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative  
30   disease states and behavioural disorders such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder and panic disorder. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:84 and may have been publicly available  
35   prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention

are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1135 of SEQ ID NO:84, b is an integer of 15 to 1149, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:84, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 75

When tested against a K562 kidney cell line, supernatants removed from cells containing this gene activated the ISRE (interferon-sensitive responsive element) pathway. Thus, it is likely that this gene activates kidney cells through the Jaks-STAT signal transduction pathway. The ISRE is a promoter element found upstream in many genes which are involved in the Jaks-STAT pathway. The Jaks-STAT pathway is a complex, signal transduction pathway involved in the differentiation and proliferation of cells. Therefore, activation of the Jaks-STATs pathway, reflected by the binding of the GAS element, can be used to indicate proteins involved in the proliferation and differentiation of cells.

This gene is expressed primarily in bone marrow and spleen.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, autoimmune diseases, transplant rejection and immunodeficiency disease states. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the hematopoietic and immune systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., bone marrow, cells and tissue of the immune system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:224 as residues: Pro-22 to His-33, Ser-42 to Trp-48.

The tissue distribution of this gene predominantly in hematopoietic cell types indicates that polynucleotides and polypeptides corresponding to this gene are important for the treatment or detection of immune or hematopoietic disorders including



arthritis, asthma, immunodeficiency diseases, leukemia, and transplant rejection. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:85 and may have been publicly available prior to conception of the present invention.

- 5 Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 753 of SEQ ID NO:85, b is an integer of 15 to 767, where  
 10 both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:85, and where b is greater than or equal to a + 14.

#### 15 FEATURES OF PROTEIN ENCODED BY GENE NO: 76

- In specific embodiments, polypeptides of the invention comprise the sequence: SLQYRIRIPGRPT (SEQ ID NO:366), DLVTYTSSLQYRIRIPGRPTRP (SEQ ID NO:367), VKTAECYSIPLGSCPVNQRVR (SEQ ID NO:369), and/or LGNKKYIN IRCLEMQVTLKILCEIEKKERRGTHCLV (SEQ ID NO:368). Polynucleotides  
 20 encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in primary dendritic cells.

- Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are  
 25 not limited to, auto-immune disorders such as asthma and arthritis, in transplant rejection, leukemia and immunodeficiency disease states. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene  
 30 at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., dendritic cells and other cells and tissue of the nervous system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level  
 35 in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:225 as residues: Gly-2 to Glu-7, Arg-27 to Gly-34.

The tissue distribution of this gene predominantly in hematopoietic cell types indicates that polynucleotides and polypeptides corresponding to this gene are important for the treatment or detection of immune or hematopoietic disorders including arthritis, asthma, immunodeficiency diseases, leukemia, hypersensitivity and graft rejection. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:86 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 714 of SEQ ID NO:86, b is an integer of 15 to 728, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:86, and where b is greater than or equal to a + 14.

#### FEATURES OF PROTEIN ENCODED BY GENE NO: 77

This gene is expressed primarily in 12 week old early stage human. Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, developmental abnormalities. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the developmental system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., developing and/or differentiating cells and tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:226 as residues: Thr-14 to Thr-19.

The expression of this gene primarily in the embryo, indicates a key role in embryo development and could be used in the treatment and or detection of developmental disorders. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences

are related to SEQ ID NO:87 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or  
5 more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 721 of SEQ ID NO:87, b is an integer of 15 to 735, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:87, and where b is greater than or equal to a + 14.

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#### FEATURES OF PROTEIN ENCODED BY GENE NO: 78

This gene is expressed primarily in T-cells, and to a lesser extent in cord blood and osteosarcoma.

15 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, auto-immune diseases, immunodeficiency diseases and host-graft rejection. Similarly, polypeptides and antibodies directed to these polypeptides are  
20 useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., cells and tissue of the immune system, and bone, and cancerous and wounded tissues) or bodily fluids (e.g.,  
25 serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:227 as residues: Pro-36 to Ala-41.

30 The expression of this gene in T-cells indicates a potential role in the treatment/detection of immune disorders such as such as arthritis, asthma, immune deficiency diseases such as AIDS, leukemia and transplant rejection. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:88 and  
35 may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly,

preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 875 of SEQ ID NO:88, b is an integer of 15 to 889, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID  
5 NO:88, and where b is greater than or equal to a + 14.

#### FEATURES OF PROTEIN ENCODED BY GENE NO: 79

10 This gene is expressed primarily in placenta and 9 week old embryo and to a lesser extent in fetal spleen.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are  
15 not limited to, developmental disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the developmental system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g.,  
20 developing and differentiating tissues, and spleen and other cells and tissue of the immune system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not  
25 having the disorder.

The expression of this gene primarily in the embryo, indicates a key role in embryo development and could be used in the treatment and or detection of developmental disorders. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences  
30 are related to SEQ ID NO:89 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general  
35 formula of a-b, where a is any integer between 1 to 555 of SEQ ID NO:89, b is an integer of 15 to 569, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:89, and where b is greater than or equal to a + 14.

**FEATURES OF PROTEIN ENCODED BY GENE NO: 80**

5           This gene is expressed primarily in early stage brain.

          Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, developmental and neurodegenerative diseases of the brain and nervous  
10       system. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the brain, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., brain and other tissue of the nervous system, and  
15       cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

          The tissue distribution indicates that polynucleotides and polypeptides  
20       corresponding to this gene are useful for the treatment and detection of developmental and neurodegenerative diseases, as well as behavioral or nervous system disorders. Examples of such conditions would include: depression, schizophrenia, mania, dementia, paranoia, addictive behavior and sleep disorders. In addition a brain-specific gene product may be useful in the diagnosis of specific brain tumors. Many  
25       polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:90 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly,  
30       preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 320 of SEQ ID NO:90, b is an integer of 15 to 334, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:90, and where b is greater than or equal to a + 14.

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**FEATURES OF PROTEIN ENCODED BY GENE NO: 81**

This gene is expressed primarily in synovial tissue.

Therefore, polynucleotides and polypeptides of the invention are useful as  
5 reagents for differential identification of the tissue(s) or cell type(s) present in a  
biological sample and for diagnosis of diseases and conditions which include, but are  
not limited to, arthritis, tendonitis and chondromalacia. Similarly, polypeptides and  
antibodies directed to these polypeptides are useful in providing immunological probes  
for differential identification of the tissue(s) or cell type(s). For a number of disorders  
10 of the above tissues or cells, particularly of the synovium, expression of this gene at  
significantly higher or lower levels may be routinely detected in certain tissues (e.g.,  
synovial tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum,  
plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken  
from an individual having such a disorder, relative to the standard gene expression  
15 level, i.e., the expression level in healthy tissue or bodily fluid from an individual not  
having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides  
corresponding to this gene are useful for the treatment and diagnosis of connective  
tissue disorders such as arthritis, tendonitis, chondromalacia, inflammation and  
20 trauma. Many polynucleotide sequences, such as EST sequences, are publicly available  
and accessible through sequence databases. Some of these sequences are related to SEQ  
ID NO:91 and may have been publicly available prior to conception of the present  
invention. Preferably, such related polynucleotides are specifically excluded from the  
scope of the present invention. To list every related sequence is cumbersome.  
25 Accordingly, preferably excluded from the present invention are one or more  
polynucleotides comprising a nucleotide sequence described by the general formula of  
a-b, where a is any integer between 1 to 781 of SEQ ID NO:91, b is an integer of 15 to  
795, where both a and b correspond to the positions of nucleotide residues shown in  
SEQ ID NO:91, and where b is greater than or equal to a + 14.

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**FEATURES OF PROTEIN ENCODED BY GENE NO: 82**

This gene is expressed primarily in frontal cortex of brain.

35 Therefore, polynucleotides and polypeptides of the invention are useful as  
reagents for differential identification of the tissue(s) or cell type(s) present in a  
biological sample and for diagnosis of diseases and conditions which include, but are

not limited to, developmental and neurodegenerative diseases of the brain . Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., brain and other tissue of the nervous system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:231 as residues: Ser-4 to Tyr-13.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection and treatment of developmental and neurodegenerative diseases of the brain and nervous system, including malignancies as well as behavioral disorders. Examples of such conditions might include: depression, schizophrenia, Alzheimer's disease, Parkinson's disease, Huntington's disease, mania, dementia, paranoia, addictive behavior and sleep disorders. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:92 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 563 of SEQ ID NO:92, b is an integer of 15 to 577, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:92, and where b is greater than or equal to a + 14.

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### FEATURES OF PROTEIN ENCODED BY GENE NO: 83

The translation product of this gene shares sequence homology with the L6 cell surface antigen, which is highly expressed in lung, breast, colon, and ovarian carcinomas. See e.g., Marken et al., Proc Natl Acad Sci U S A 1992 Apr 15;89(8):3503-3507. In a specific embodiment, polypeptides of the invention comprise

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the sequence: ITLCLVCIVANA (SEQ ID NO:370). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in tissues of liver origin (fetal liver, hepatoma, hepatocellular tumor).

- 5 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cancers of the liver. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential
- 10 identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the hepatic system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., lung and pulmonary tissue, colon and other gastrointestinal tissue, mammary tissue, ovarian tissue and other tissue of the reproductive system, and hepatic tissue, and
- 15 cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:232 as residues:
- 20 Asn-32 to Asn-41, Thr-140 to Ala-147, Asp-188 to His-197.

- The murine monoclonal antibody (mAb) L6 recognizes an integral membrane glycoprotein that is highly expressed in lung, breast, colon, and ovarian carcinomas and is referred to as the L6 antigen. This antigen is an attractive target for therapeutic intervention due to its high level expression on malignant cells. The tissue distribution
- 25 and homology to L6 antigen indicates that the protein product of this gene is useful for detection and treatment of neoplastic tissues -- particularly of the liver. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:93 and may have been publicly available prior to conception of the present invention.
- 30 Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 954 of SEQ ID NO:93, b is an integer of 15 to 968, where
- 35 both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:93, and where b is greater than or equal to a + 14.



**FEATURES OF PROTEIN ENCODED BY GENE NO: 84**

5           This gene is expressed primarily in glioblastoma.

          Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, glioblastoma. Similarly, polypeptides and antibodies directed to these  
10   polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., cells and tissue of the nervous system, and cancerous and wounded tissues) or bodily fluids (e.g., serum,  
15   plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

          The tissue distribution indicates that polynucleotides and polypeptides  
20   corresponding to this gene are useful for the detection and treatment of malignancies, as well as developmental and neurodegenerative diseases of the brain and nervous system. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:94 and may have been publicly available prior to conception of the present  
25   invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 539 of SEQ ID NO:94, b is an integer of 15 to  
30   553, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:94, and where b is greater than or equal to a + 14.

**FEATURES OF PROTEIN ENCODED BY GENE NO: 85**

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          The translation product of this gene shares sequence homology with Tbx which is thought to be important in developmental regulation (see e.g., Knezevic et al.,

Development 124: 411-419 (1997); accession No. U80951). In specific embodiments, polypeptides of the invention comprise the sequence: VTAYQNQQITRLKIDRNPFAGFR (SEQ ID NO:371), GTATVTAYQ NQQITRL (SEQ ID NO:372), KIDRNPFAGFRDSGRNRMGLEAL (SEQ ID NO:373), VESYAFWRPSLRTLTFEDIPGIPKQGNASS (SEQ ID NO:375), and/or  
5 STLLQVLGMAFLPLTLTFCLA (SEQ ID NO:374). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in synovial sarcoma and to a lesser extent in osteoclastoma and hemangiopericytoma.

10 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, osteosarcoma, osteoclastoma, chondrosarcoma. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological  
15 probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the skeletal system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., bone cells and tissue, and synovial cells and tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial  
20 fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:234 as residues: Ala-45 to Asp-50, Arg-57 to Pro-63.

25 The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of osteoporosis, fracture, osteosarcoma, osteoclastoma, chondrosarcoma, ossification and osteonecrosis, arthritis, tendonitis, chondromalacia, inflammation. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through  
30 sequence databases. Some of these sequences are related to SEQ ID NO:95 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a  
35 nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 954 of SEQ ID NO:95, b is an integer of 15 to 968, where both a and b

correspond to the positions of nucleotide residues shown in SEQ ID NO:95, and where b is greater than or equal to a + 14.

## 5 FEATURES OF PROTEIN ENCODED BY GENE NO: 86

This gene maps to chromosome 19, accordingly, polynucleotides of the invention may be used in linkage analysis as a marker for chromosome 19. The translation product of this gene is a transmembrane protein that forms disulfide-bonded  
 10 homodimers and contains a motif in its cytoplasmic domain (located at the carboxy terminus of the protein relative to the transmembrane domain) that functions as an adaptor for associating protein complexes involved in triggering cellular activation. The transmembrane domain is predicted to consist of the amino acid sequence: VLAGIVMGDLVLTVLIALAVYFLG (SEQ ID NO:377). In specific embodiments,  
 15 polypeptides of the invention comprise, or alternatively, consist of, the sequence: QAQSDCSCSTVSPG (SEQ ID NO:376), VLAGIVMGDLVLTVLIALA VYFLG (SEQ ID NO:377), VPRGRGAAEATRKRITETESPYQELQGQRSDVYSDL (SEQ ID NO:378), and/or ETESPYQELQGQRSDVYSDLNT (SEQ ID NO:379). Polynucleotides encoding these polypeptides are also encompassed by the invention.

20 This gene is expressed primarily in macrophages.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immunologically mediated disorders. Similarly, polypeptides and  
 25 antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., blood cells, and cells and tissue of the immune system, and cancerous  
 30 and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:235 as residues:  
 35 Ala-28 to Ser-33, Ala-76 to Lys-111.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of immune

disorders including: leukemias, lymphomas, auto-immunities, immunodeficiencies (e.g., AIDS), immuno-suppressive conditions (transplantation) and hematopoietic disorders. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are  
5 related to SEQ ID NO:96 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of  
10 a-b, where a is any integer between 1 to 683 of SEQ ID NO:96, b is an integer of 15 to 697, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:96, and where b is greater than or equal to a + 14.

#### 15 FEATURES OF PROTEIN ENCODED BY GENE NO: 87

This gene is expressed primarily in prostate cancer.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a  
20 biological sample and for diagnosis of diseases and conditions which include, but are not limited to, prostate cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the prostate, expression of this gene at significantly higher or lower  
25 levels may be routinely detected in certain tissues (e.g., prostate, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

30 The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for detection and treatment of prostate cancer and other prostate disorders. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:97 and may have been publicly available prior to conception  
35 of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or

more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 852 of SEQ ID NO:97, b is an integer of 15 to 866, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:97, and where b is greater than or equal to a + 14.

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## FEATURES OF PROTEIN ENCODED BY GENE NO: 88

The translation product of this gene shares sequence homology with retinal epithelial membrane protein (REMP), which is thought to be important in development and maintenance of normal retinal function (See e.g., Philp et al., Exp. Cell Res. 219 (1), 64-73 (1995); and accession no.U15685). The translation product of this gene also shares homology with monocarboxylate transporter protein (accession no.U87627). In specific embodiments, polypeptides of the invention comprise, or alternatively, consist of, the sequence: FLCALSPLGQLLQDRYGWRGGFLILGGL (SEQ ID NO:380), LLNCCVCAALMRPLVVTAQPGXGPPRP (SEQ ID NO:381), and/or SRRLXDLSV FRDRGFVLYAVAASVM (SEQ ID NO:382). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in neutrophils and to a lesser extent in a variety of other tissues and cell types, including retina.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, eye disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the eye, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., retinal cells and other cells and tissue of the nervous system, neutrophils and other blood cells, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology to REMP indicates polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of eye disorders, including neoplasms, visual impairments and blindness. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible

through sequence databases. Some of these sequences are related to SEQ ID NO:98 and may have been publicly available prior to conception of the present invention.

Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly,

- 5 preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1354 of SEQ ID NO:98, b is an integer of 15 to 1368, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:98, and where b is greater than or equal to a + 14.

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### FEATURES OF PROTEIN ENCODED BY GENE NO: 89

- 15 The translation product of this gene shares sequence homology with human squamous cell E48 antigen which is thought to be important in self-recognition, immune function. Additional embodiments of the invention are directed to polypeptides comprising the sequence:

- MMATPSTRPPPPAASTTSATAPALPPRPPWPWPPSSWPPSGVSSKAPEADPLK  
NKAL (SEQ ID NO:383); LLLTSPLPRCPPACSHDAPAHDPGPGPHGLTSGPGLG  
20 LPRVCLQRRQLLQPHALPGYGCLLDHAHLLHPHQDEGQ (SEQ ID NO:384);  
and/or WLLQARVHHLLLPVRPLQRHRPCHPGHPGPGHPPGHPLGSPLKPP  
RQTHSRTKLS (SEQ ID NO:385). Further embodiments of the invention include polynucleotides encoding these polypeptides.

- 25 This gene is expressed primarily in adult brain and to a lesser extent in fetal lung.

- Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, autoimmune disorders. Similarly, polypeptides and antibodies directed to  
30 these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., brain and other cells and tissue of the immune system, lung, and cancerous and  
35 wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue

or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:238 as residues: Tyr-28 to Phe-34, Thr-54 to Val-60, Tyr-73 to Thr-82.

- The tissue distribution and homology to human squamous cell E48 antigen
- 5 indicates that the polynucleotides and polypeptides corresponding to this gene are useful for study, diagnosis and treatment of autoimmune diseases and disorders. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:99 and may have been publicly available prior to conception of the present invention.
- 10 Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 599 of SEQ ID NO:99, b is an integer of 15 to 613, where
- 15 both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:99, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 90

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Additional embodiments of the invention include polypeptides comprising of the following amino acid sequences:

- QEFQTGLGNMVKPCLYEKYRNISWLWWHTPVVPATWEAEVGGSLPEGRRLRLQ  
(SEQ ID NO:386) and/or ILGGESILILSWVFSYIFFRIALEITIYILNVSPFCLG
- 25 RWLM PVIPALWEAEVGGGLPELRSSRPA (SEQ ID NO:387). Further embodiments include polynucleotides encoding these polypeptides.

This gene is expressed primarily in human adult lymph node tissue.

- Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a
- 30 biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune disorders and lymphomas. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and metabolic systems,
- 35 expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., lymph tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or

cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for study, diagnosis and treatment of immune and lymph diseases and disorders such as lymphomas. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:100 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 671 of SEQ ID NO:100, b is an integer of 15 to 685, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:100, and where b is greater than or equal to a + 14.

#### FEATURES OF PROTEIN ENCODED BY GENE NO: 91

Additional embodiments of the invention include polypeptides comprising of the following amino acid sequences: MPKQLAQLLYRLPRG (SEQ ID NO:388); LFQAIS VSGSHRQGSRTWNTLTEGNAEAACTVALQTSKRLILASRW (SEQ ID NO:389); TLSFMNSHCVPKALFFLSVVSYIFIMPHHFFTVKILKSCFQVGQLMKL (SEQ ID NO:390); and/or RPTRPITFSSNISEWVPSTGFQDLEHFNRRKCRSS LHSCFTDFQEADSGFKMEPWSWFFFFFFFFFPQRTCGCALCVLFLFSIW GPHGKELLNSFLYELPLCSYKGPFLS (SEQ ID NO:391). Further embodiments of the invention are directed to polynucleotides which encode these polypeptides.

This gene is expressed primarily in placenta and synovium.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases of the synovium and placenta. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the placenta and synovium, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., synovial tissue, and cancerous and



wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

5           The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for study, diagnosis and treatment of growth and development disorders and arthritic and inflammatory conditions. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:101 and may  
10       have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer  
15       between 1 to 632 of SEQ ID NO:101, b is an integer of 15 to 646, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:101, and where b is greater than or equal to a + 14.

## 20       **FEATURES OF PROTEIN ENCODED BY GENE NO: 92**

Additional embodiments of the invention include polypeptides comprising the following amino acid sequences:

25       VDPRVRLPLFWWQPSCAVYLFPRVYNNMCTRVLGTLPHCWDLATLLQPSSRI  
WGNVSEAPGM (SEQ ID NO:392); VPYHIAGTLPHCCSLPVGYGGMSVRL  
QGCRYVGNVGPQGNMQSGRSWALKMVLLCNSCLGLGVGSVGPSMSSLF  
GAVLSETPGSSVY (SEQ ID NO:393); and/or MLDPRATCNLVGVGLS  
KWCCCVTAAWVLG (SEQ ID NO:394). Further embodiments of the invention  
include polynucleotides which encode these polypeptides.

30       This gene is expressed primarily in chronic lymphocytic leukemia.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases of immune system including cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in  
35       providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be

5 routinely detected in certain tissues (e.g., cells and tissue of the immune system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for study, diagnosis and treatment of disorders of the immune system including cancers. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:102 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 812 of SEQ ID NO:102, b is an integer of 15 to 826, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:102, and where b is greater than or equal to a + 14.

## 20 FEATURES OF PROTEIN ENCODED BY GENE NO: 93

Additional embodiments of the invention include polypeptides comprising of the following amino acid sequences:  
 HGDWYIVHIVEQLNQANNKSVTSHTYFVVKTCKIHSLSNFQASNTLLXTVVTM  
 25 LYNRSLELILPV (SEQ ID NO:395); TYSSCLTKILYSLINIPIPHCSPAXITIL  
 LSASMNLTFFFFRFHICEIAQYLSFCAWLISLNIKSL (SEQ ID NO:396); and/or  
 MNLTFFFFRFHICEIAQYLSFCAWLISLNIKSL (SEQ ID NO:397). Further  
 embodiments include polynucleotides which encode these polypeptides.

This gene is expressed primarily in brain medulloblastoma.  
 30 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of cancer and disorders of the CNS. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a  
 35 number of disorders of the above tissues or cells, particularly of the central nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., brain and other cells and tissue of the nervous system,

and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of cancers and other disorders and diseases of the CNS. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:103 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 572 of SEQ ID NO:103, b is an integer of 15 to 586, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:103, and where b is greater than or equal to a + 14.

## 20 FEATURES OF PROTEIN ENCODED BY GENE NO: 94

Additional embodiments of the invention include polypeptides comprising the following amino acid sequences:  
LVCYCSTKKEKKLHEIAIQQGQNWRWLLFYKEISVPGFQSVWCSYKCLCVVW  
25 KAGEGG (SEQ ID NO:398); RRSCSGPPLVNTAGKILSSSPAKLACKRTDFHIPS  
(SEQ ID NO:399); RASILGIDNERGCHFRHFNPLKEYKRKKKENKSFRIV (SEQ  
ID NO:400); SKNKTRGGDWCVTVLRKRRKSFMSKPFSDRTGDGFSFTKKS  
LSQAFSLFGVHTSVCVLCGRRGKAGEGGPVQGGLW (SEQ ID NO:401); and/or  
MKSPFSKDRTGDGFSFTKKSLSQAFSLFGVHTSVCVLCGRRGKAGEGGPVQG  
30 PLW (SEQ ID NO:402). Further embodiments include polynucleotides comprising these amino acid sequences.

This gene is expressed primarily in meningioma and neutrophils and to a lesser extent in anergic T cells and CD34 depleted buffy coat.

Therefore, polynucleotides and polypeptides of the invention are useful as  
35 reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, inflammatory, immune and hemopoietic disorders. Similarly,

polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the hemopoietic, immune and inflammatory systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., T-cells and other cells and tissue of the immune system, meningima, neutrophils and other blood cells, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:243 as residues: Glu-45 to Asn-50.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the study, diagnosis and treatment of various disorders and diseases of the immune, inflammatory, and hemopoietic systems. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:104 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 614 of SEQ ID NO:104, b is an integer of 15 to 628, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:104, and where b is greater than or equal to a + 14.

#### FEATURES OF PROTEIN ENCODED BY GENE NO: 95

Additional embodiments of the invention include polypeptides comprising the following amino acid sequences: MGESECYRRLSGASCTWTVHVDFA (SEQ ID NO:403); MHCGRVWKTMKHDYFLLACLSMTSTGGILCTL (SEQ ID NO:404); STLSLIPTSSSLFWPWCTAIIGSIFTYCVCVCVCFVVMNRTCYPNSIHYHNSKL ATIDKSM TLS (SEQ ID NO:405); and/or MWILPKVSLICIVELGYGKP (SEQ ID NO:406). Further embodiments include polynucleotides encoding these polypeptides.

This gene is expressed primarily in human meningima.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, meningitis and other inflammatory conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the cerebrospinal membranes, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., meningima, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:244 as residues: Ser-35 to Phe-41.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for study, treatment, and diagnosis of disorders of the meningima. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:105 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 544 of SEQ ID NO:105, b is an integer of 15 to 558, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:105, and where b is greater than or equal to a + 14.

#### FEATURES OF PROTEIN ENCODED BY GENE NO: 96

Additional embodiments of the invention are directed to polypeptides comprising the following amino acid sequences:  
 MSTGDGRDAEKGWVPVSEENQRSVYPGYPECDERQAVPQHCAIASPSSLQSHH  
 PASACVPRR (SEQ ID NO:407); QQMTLGTIKIKWGLQRGQEPTGDFTVR  
 NFMRFSI IYC (SEQ ID NO:408); and/or PFLFCASRIRXQGIGIHGQ  
 VACSAVRMYNNR (SEQ ID NO:409). Further embodiments of the invention are directed to polynucleotides which encode these polypeptides.

This gene is expressed primarily in activated monocytes.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune and hematopoietic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and hemopoietic systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., monocytes and other cells and tissue of the immune system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:245 as residues: Met-1 to Ser-6, Pro-29 to Ser-34.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for study, diagnosis and treatment of diseases of the immune and hemopoietic systems. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:106 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 742 of SEQ ID NO:106, b is an integer of 15 to 756, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:106, and where b is greater than or equal to a + 14.

30

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 97**

Additional embodiments of the invention are directed to polypeptides comprising the following amino acid sequences:

35 VLCEEAGQKVPSTPSWSSWTLQKRLRGSPA EANCSPSPAPPGKE (SEQ ID NO:410); MSLSALACDFT PIQPWEWEEYEQITLGLTAPSNLLESNYLGQASECFV RKLVRFPQLLP GPPGHCRKDLGDPQQRPIALLPSLPHQERNNVHRLEADSEV

DL (SEQ ID NO:411); CVDFDEYFSSWEPLLKMMFKGVVGGKMKAWRRKKR  
RKPLPYKIHAD (SEQ ID NO:412); and/or MMFKGVVGGKMKAWRRK  
KRRKPLPYKIHAD (SEQ ID NO:413). Further embodiments of the invention are  
directed to polynucleotides which encode these polypeptides.

5 This gene is expressed primarily in bone marrow and to a lesser extent in testes.

Therefore, polynucleotides and polypeptides of the invention are useful as  
reagents for differential identification of the tissue(s) or cell type(s) present in a  
biological sample and for diagnosis of diseases and conditions which include, but are  
not limited to, hemopoietic and reproductive disorders. Similarly, polypeptides and  
10 antibodies directed to these polypeptides are useful in providing immunological probes  
for differential identification of the tissue(s) or cell type(s). For a number of disorders  
of the above tissues or cells, particularly of the hemopoietic and reproductive systems,  
expression of this gene at significantly higher or lower levels may be routinely detected  
in certain tissues (e.g., bone marrow, testes and other reproductive tissue, and  
15 cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial  
fluid and spinal fluid) or another tissue or cell sample taken from an individual having  
such a disorder, relative to the standard gene expression level, i.e., the expression level  
in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides  
20 corresponding to this gene are useful for study, diagnosis and treatment of various  
disorders involving the hemopoietic and reproductive systems. Many polynucleotide  
sequences, such as EST sequences, are publicly available and accessible through  
sequence databases. Some of these sequences are related to SEQ ID NO:107 and may  
have been publicly available prior to conception of the present invention. Preferably,  
25 such related polynucleotides are specifically excluded from the scope of the present  
invention. To list every related sequence is cumbersome. Accordingly, preferably  
excluded from the present invention are one or more polynucleotides comprising a  
nucleotide sequence described by the general formula of a-b, where a is any integer  
between 1 to 1132 of SEQ ID NO:107, b is an integer of 15 to 1146, where both a and  
30 b correspond to the positions of nucleotide residues shown in SEQ ID NO:107, and  
where b is greater than or equal to a + 14.

### FEATURES OF PROTEIN ENCODED BY GENE NO: 9°

35

Additional embodiments of the invention are directed to polypeptides  
comprising the following amino acid sequences:

LISSVNKTKQKRSDATLSHKHDRLLNHFVFFGNSYNY (SEQ ID NO:414);  
SSKFPS  
DMLLRIQQIIYCHKLTIILTKWRNTARHKSKKKEDELILKHELQLKKWKNRLIL  
KRAAAEESNFPERSSEVFLVDETLKCDISLLPEXAILQVCMNSVYIIYYNLPSVV  
5 VHACNPSCCLGG (SEQ ID NO:415); SLESTNAIKSN (SEQ ID NO:416);  
IRPNKNDQMRHCLINMIDY (SEQ ID NO:417); ITLCFLETAITINIYSNL  
VNFLQICYCGYNRSSIVTS (SEQ ID NO:418); and/or ISFRYAIADTTDHLLSQA  
NHYPNKMAEYSKT (SEQ ID NO:419). Further embodiments of the invention are  
directed to polynucleotides which encode these polypeptides.

10 This gene is expressed primarily in nasal polyps.

Therefore, polynucleotides and polypeptides of the invention are useful as  
reagents for differential identification of the tissue(s) or cell type(s) present in a  
biological sample and for diagnosis of immune system disorders. Similarly,  
polypeptides and antibodies directed to these polypeptides are useful in providing  
15 immunological probes for differential identification of the tissue(s) or cell type(s). For a  
number of disorders of the above tissues or cells, particularly of the immune and  
respiratory systems, expression of this gene at significantly higher or lower levels may  
be routinely detected in certain tissues (e.g., nasal tissue, and cancerous and wounded  
tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or  
20 another tissue or cell sample taken from an individual having such a disorder, relative to  
the standard gene expression level, i.e., the expression level in healthy tissue or bodily  
fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides  
corresponding to this gene are useful for diagnosis and treatment of disorders of the  
25 immune system. Many polynucleotide sequences, such as EST sequences, are publicly  
available and accessible through sequence databases. Some of these sequences are  
related to SEQ ID NO:108 and may have been publicly available prior to conception of  
the present invention. Preferably, such related polynucleotides are specifically excluded  
from the scope of the present invention. To list every related sequence is cumbersome.  
30 Accordingly, preferably excluded from the present invention are one or more  
polynucleotides comprising a nucleotide sequence described by the general formula of  
a-b, where a is any integer between 1 to 761 of SEQ ID NO:108, b is an integer of 15  
to 775, where both a and b correspond to the positions of nucleotide residues shown in  
SEQ ID NO:108, and where b is greater than or equal to a + 14.



**FEATURES OF PROTEIN ENCODED BY GENE NO: 99**

An additional embodiment of the invention is directed to polypeptides comprising those which exhibit sequence homology with honeybee venom sacepin.

- 5 Further embodiments of the invention are directed to polynucleotides which encode these polypeptides. Additional embodiments of the invention are directed to polypeptides comprising the following amino acid sequences:

PQIKLLNSDALGMRTTSXDLVPCNQCFIPLPPSCNRIASRKAVNWKQQR LPAVR  
 GLLNNAPHRRPPTPRTPCVFPSEGPKGYGFHV (SEQ ID NO:420); EQLAXISCR  
 10 VINVSFRCLHHVIESLPERQLTGSSRGSQP (SEQ ID NO:421); EDCSTMPPI  
 AAPPPLAPLVFSPLRGPRVMAFMSRCGDRGGRGRSXAGRGWPWSESGVINAH  
 PKKRPCPGMLS (SEQ ID NO:422); and/or EFGTRRQWGTR CFPPLVGRKQ  
 SALRRREGKARAGRCCGKRSVKAGFDA (SEQ ID NO:423). Further embodiments  
 of the invention are directed to polynucleotides which encode these polypeptides.

- 15 This gene is expressed primarily in activated and control neutrophils and to a lesser extent in fetal liver and spleen.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of disorders of the immune and endocrine systems.

- 20 Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune, inflammatory and hormonal systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., neutrophils and  
 25 other blood cells, spleen and other cells and tissue of the immune system, liver, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

- 30 The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for study, diagnosis and treatment of inflammation and various disorders of the immune and endocrine systems. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:109  
 35 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly,

preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 897 of SEQ ID NO:109, b is an integer of 15 to 911, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:109, and where b is greater than or equal to a + 14.

#### FEATURES OF PROTEIN ENCODED BY GENE NO: 100

10 This gene is expressed primarily in activated neutrophils.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune disorders, inflammation. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., neutrophils and other blood cells, and cells and tissue of the immune system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

20 The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for study and treatment of inflammatory and immune conditions. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:110 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 442 of SEQ ID NO:110, b is an integer of 15 to 456, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:110, and where b is greater than or equal to a + 14.

**FEATURES OF PROTEIN ENCODED BY GENE NO: 101**

Additional embodiments of the invention are directed to polypeptides  
 5 comprising the following amino acid  
 sequences: ATVPGSIYNYFYHYNAGALKPEHASESPRGLCAQTAGPFPSF (SEQ  
 ID NO:424); IRHEPPPPRFKRFSCLSLLSSWDYRRAPPHVAIFCTLSRDGVLPHW  
 PGWSQTPDLK (SEQ ID NO:425); STHLGLPRCWDYRHEPLCLAPFTTISIIMQ  
 GLSNLSMPQNPEGCAHRLDLSPASDSVPPEWGSKIAFEV (SEQ ID NO:426);  
 10 and/or LRVGGTSENCCRGECCGVCIPPGR (SEQ ID NO:427). Further  
 embodiments of the invention are directed to polynucleotides which encode these  
 polypeptides.

This gene is expressed primarily in neutrophils.

Therefore, polynucleotides and polypeptides of the invention are useful as  
 15 reagents for differential identification of the tissue(s) or cell type(s) present in a  
 biological sample and for diagnosis of diseases and conditions which include, but are  
 not limited to, immune disorders. Similarly, polypeptides and antibodies directed to  
 these polypeptides are useful in providing immunological probes for differential  
 identification of the tissue(s) or cell type(s). For a number of disorders of the above  
 20 tissues or cells, particularly of the immune system, expression of this gene at  
 significantly higher or lower levels may be routinely detected in certain tissues (e.g.,  
 neutrophils and other blood cells, and cells and tissue of the immune system, and  
 cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial  
 fluid and spinal fluid) or another tissue or cell sample taken from an individual having  
 25 such a disorder, relative to the standard gene expression level, i.e., the expression level  
 in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides  
 corresponding to this gene are useful for study and treatment of immune disorders.  
 Many polynucleotide sequences, such as EST sequences, are publicly available and  
 30 accessible through sequence databases. Some of these sequences are related to SEQ ID  
 NO:111 and may have been publicly available prior to conception of the present  
 invention. Preferably, such related polynucleotides are specifically excluded from the  
 scope of the present invention. To list every related sequence is cumbersome.  
 Accordingly, preferably excluded from the present invention are one or more  
 35 polynucleotides comprising a nucleotide sequence described by the general formula of  
 a-b, where a is any integer between 1 to 540 of SEQ ID NO:111, b is an integer of 15

to 554, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:111, and where b is greater than or equal to a + 14.

## 5 FEATURES OF PROTEIN ENCODED BY GENE NO: 102

This gene is expressed primarily in neutrophils.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., neutrophils and other blood cells, and cells and tissue of the immune system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:251 as residues: Lys-33 to Lys-41.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for study and treatment of immune disorders. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:112 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 708 of SEQ ID NO:112, b is an integer of 15 to 722, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:112, and where b is greater than or equal to a + 14.

**FEATURES OF PROTEIN ENCODED BY GENE NO: 103**

This gene is expressed primarily in neutrophils.

Therefore, polynucleotides and polypeptides of the invention are useful as  
5 reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential  
10 identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., neutrophils and other blood cells, and cells and tissue of the immune system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having  
15 such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for study and treatment of immune disorders. Many polynucleotide sequences, such as EST sequences, are publicly available and  
20 accessible through sequence databases. Some of these sequences are related to SEQ ID NO:113 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more  
25 polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 917 of SEQ ID NO:113, b is an integer of 15 to 931, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:113, and where b is greater than or equal to a + 14.

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**FEATURES OF PROTEIN ENCODED BY GENE NO: 104**

Additional embodiments of the invention are directed to polypeptides comprising the following amino acid  
35 sequences:GLCMVHSLLTSSLGGRCCNYPYIADKDIETEVK PPSQGHTWHLHCS (SEQ ID NO:428); QLWCITALPSTRHCSKGFAWFTHSLRH PSVAGAVIILQTRTLRQRSSHLPGTHGICTAPDRPTERRAAVTILK (SEQ ID NO:429); SFDNN

NSYGVSQLYQVPDTVLRALHGSLTPYVIPRWQVL (SEQ ID NO:430); and/or DRGQATFP RAHMASALLLTDRQRELLSRSSNELCMSKV (SEQ ID NO:431). Further embodiments of the invention are directed to polynucleotides which encode these polypeptides.

5 This gene is expressed primarily in neutrophils.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of immune diseases and disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing  
10 immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., neutrophils and other blood cells, and cells and tissue of the immune system, and cancerous and wounded tissues) or bodily fluids (e.g., serum,  
15 plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides  
20 corresponding to this gene are useful for study and treatment of immune disorders. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:114 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the  
25 scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 574 of SEQ ID NO:114, b is an integer of 15 to 588, where both a and b correspond to the positions of nucleotide residues shown in  
30 SEQ ID NO:114, and where b is greater than or equal to a + 14.

#### FEATURES OF PROTEIN ENCODED BY GENE NO: 105

35 Additional embodiments of the invention are directed to polypeptides comprising the following amino acid sequences:  
LLLLRPFLNSQFKLQLPLVLFHSSCTYICLLYNYELFHIVALTGKLMNGLHLF

AHHLILAVAHXGCSIPIY (SEQ ID NO:432); and/or THNSNYSSLWFSST  
 AVVLTYYVYYIIMNCFILSPLQVN (SEQ ID NO:433). Further embodiments of the  
 invention are directed to polynucleotides which encode these polypeptides.

This gene is expressed primarily in neutrophils.

5 Therefore, polynucleotides and polypeptides of the invention are useful as  
 reagents for differential identification of the tissue(s) or cell type(s) present in a  
 biological sample and for diagnosis of immune disorders and diseases. Similarly,  
 polypeptides and antibodies directed to these polypeptides are useful in providing  
 immunological probes for differential identification of the tissue(s) or cell type(s). For a  
 10 number of disorders of the above tissues or cells, particularly of the immune system,  
 expression of this gene at significantly higher or lower levels may be routinely detected  
 in certain tissues (e.g., neutrophils and other blood cells, and cells and tissue of the  
 immune system, and cancerous and wounded tissues) or bodily fluids (e.g., serum,  
 plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken  
 15 from an individual having such a disorder, relative to the standard gene expression  
 level, i.e., the expression level in healthy tissue or bodily fluid from an individual not  
 having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides  
 corresponding to this gene are useful for study and treatment of inflammatory and  
 20 immune disorders. Many polynucleotide sequences, such as EST sequences, are  
 publicly available and accessible through sequence databases. Some of these sequences  
 are related to SEQ ID NO:115 and may have been publicly available prior to conception  
 of the present invention. Preferably, such related polynucleotides are specifically  
 excluded from the scope of the present invention. To list every related sequence is  
 25 cumbersome. Accordingly, preferably excluded from the present invention are one or  
 more polynucleotides comprising a nucleotide sequence described by the general  
 formula of a-b, where a is any integer between 1 to 798 of SEQ ID NO:115, b is an  
 integer of 15 to 812, where both a and b correspond to the positions of nucleotide  
 residues shown in SEQ ID NO:115, and where b is greater than or equal to a + 14.  
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#### FEATURES OF PROTEIN ENCODED BY GENE NO: 106

Additional embodiments of the invention are directed to polypeptides  
 35 comprising the following amino acid sequences:  
 TLVAGSPCSLSRWIMAGFCHGELVQSDMESQEWERGQVVLSTSLPWCYVSP  
 R (SEQ ID NO:434); MAGFCHGELVQSDMESQEWERGQVVLSTSLPWCYVSPR

(SEQ ID NO:435); and/or MAVWISGSYSSFCRSNWDVFSPNIVLASLPFSFRS  
VSKAAKPWWLALPALFPDGLWLDSAMGSLYSQTWKARNGKEVRWFSP  
PHCLGAMSHL (SEQ ID NO:436). Further embodiments of the invention are directed  
to polynucleotides which encode these polypeptides.

5 This gene is expressed primarily in neutrophils.

Therefore, polynucleotides and polypeptides of the invention are useful as  
reagents for differential identification of the tissue(s) or cell type(s) present in a  
biological sample and for diagnosis of immune disorders and diseases. Similarly,  
polypeptides and antibodies directed to these polypeptides are useful in providing  
10 immunological probes for differential identification of the tissue(s) or cell type(s). For a  
number of disorders of the above tissues or cells, particularly of the immune system,  
expression of this gene at significantly higher or lower levels may be routinely detected  
in certain tissues (e.g., neutrophils and other blood cells, and cells and tissue of the  
immune system, and cancerous and wounded tissues) or bodily fluids (e.g., serum,  
15 plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken  
from an individual having such a disorder, relative to the standard gene expression  
level, i.e., the expression level in healthy tissue or bodily fluid from an individual not  
having the disorder. Preferred epitopes include those comprising a sequence shown in  
SEQ ID NO:255 as residues: Pro-54 to Gly-62.

20 The tissue distribution indicates that polynucleotides and polypeptides  
corresponding to this gene are useful for study and treatment of immune disorders.  
Many polynucleotide sequences, such as EST sequences, are publicly available and  
accessible through sequence databases. Some of these sequences are related to SEQ ID  
NO:116 and may have been publicly available prior to conception of the present  
25 invention. Preferably, such related polynucleotides are specifically excluded from the  
scope of the present invention. To list every related sequence is cumbersome.  
Accordingly, preferably excluded from the present invention are one or more  
polynucleotides comprising a nucleotide sequence described by the general formula of  
a-b, where a is any integer between 1 to 492 of SEQ ID NO:116, b is an integer of 15  
30 to 506, where both a and b correspond to the positions of nucleotide residues shown in  
SEQ ID NO:116, and where b is greater than or equal to a + 14.

#### 35 FEATURES OF PROTEIN ENCODED BY GENE NO: 107

Additional embodiments of the invention are directed to polypeptides  
comprising the following amino acid sequences:



RSKRQSQGSRCVPLLAQQSRSPVPLQAQPAWLLGSETIAWSGGGSGWEGPR  
 DPGTSTAAGNSGPGIGMGHRTPPPSHTGR (SEQ ID NO:437); RWDPAWGLD  
 IPESSCPVTMGELRSGDGIVL (SEQ ID NO:438); GALLWDNSMISAPRG  
 SHREAGALFPSWLSNPAVLPSRSRPSQPGCLDPRQ (SEQ ID NO:439); NSARE  
 5 PRRWIRPTRGSGETTAPCCFEPLNGGTLVHAAAMARASEAAGTG (SEQ ID  
 NO:440); MARASE AAGTG (SEQ ID NO:441); CFTTAFQKALRDPRPTLPDTHG  
 SLRNAPLKSLTLPAAFVVSFFFLSLLQDGIKERSQTQNATFFFHDRSDIE  
 GLSEEPGSGTTP (SEQ ID NO:442); and/or LALQE AVTGKQVLCSP  
 GSAIPQSSRPAPGPASLAAWIRDNSLVWRRLRVGGTQGPQHGYSSWEFRPRD  
 10 RDGAQDTPISHREMKVGSSMGTGHP (SEQ ID NO:443). Further embodiments  
 of the invention are directed to polynucleotides which encode these polypeptides.

This gene is expressed primarily in neutrophils.

Therefore, polynucleotides and polypeptides of the invention are useful as  
 reagents for differential identification of the tissue(s) or cell type(s) present in a  
 15 biological sample and for diagnosis of immune disorders and diseases. Similarly,  
 polypeptides and antibodies directed to these polypeptides are useful in providing  
 immunological probes for differential identification of the tissue(s) or cell type(s). For a  
 number of disorders of the above tissues or cells, particularly of the immune system,  
 expression of this gene at significantly higher or lower levels may be routinely detected  
 20 in certain tissues (e.g., neutrophils and other blood cells, and cells and tissue of the  
 immune system, and cancerous and wounded tissues) or bodily fluids (e.g., serum,  
 plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken  
 from an individual having such a disorder, relative to the standard gene expression  
 level, i.e., the expression level in healthy tissue or bodily fluid from an individual not  
 25 having the disorder. Preferred epitopes include those comprising a sequence shown in  
 SEQ ID NO:256 as residues: Met-25 to Gly-30.

The tissue distribution indicates that polynucleotides and polypeptides  
 corresponding to this gene are useful for study and treatment of immune disorders.  
 Many polynucleotide sequences, such as EST sequences, are publicly available and  
 30 accessible through sequence databases. Some of these sequences are related to SEQ ID  
 NO:117 and may have been publicly available prior to conception of the present  
 invention. Preferably, such related polynucleotides are specifically excluded from the  
 scope of the present invention. To list every related sequence is cumbersome.  
 Accordingly, preferably excluded from the present invention are one or more  
 35 polynucleotides comprising a nucleotide sequence described by the general formula of  
 a-b, where a is any integer between 1 to 737 of SEQ ID NO:117, b is an integer of 15

to 751, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:117, and where b is greater than or equal to a + 14.

## 5 FEATURES OF PROTEIN ENCODED BY GENE NO: 108

Additional embodiments of the invention are directed to polypeptides comprising the following amino acid sequences:

MFYSKIFYFLLNSDTSNNVTSKTLVSSISSNNRLAVSIVF (SEQ ID NO:444);  
 10 SRQKNLLKLHSPNCDNFCFIFNYKPKYICIFKLICLKILLYIFGSG (SEQ ID NO:445); and/or MLLSLLMVFTSELYVKRHISFKSXDKPHCHKNQDIDVLFRLKLEKHFVKVINMICFP (SEQ ID NO:446). Further embodiments of the invention are directed to polynucleotides which encode these polypeptides.

This gene is expressed primarily in fetal liver and to a lesser extent in bone and  
 15 breast cancer cell lines.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cancer and metabolic disorders. Similarly, polypeptides and antibodies  
 20 directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the digestive and skeletal system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., hepatic tissue, bone, mammary tissue, and cancerous and wounded  
 25 tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides  
 30 corresponding to this gene are useful for study and treatment of growth and metabolic disorders and neoplasias. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:118 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically  
 35 excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general

formula of a-b, where a is any integer between 1 to 946 of SEQ ID NO:118, b is an integer of 15 to 960, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:118, and where b is greater than or equal to a + 14.

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#### FEATURES OF PROTEIN ENCODED BY GENE NO: 109

Additional embodiments of the invention are directed to polypeptides comprising the following amino acid sequences: FREYGFYNLHFC (SEQ ID NO:447); LVTDD YYDGCNEDYEYNWSYMFLNSEQLFKIFYPTFFC (SEQ ID NO:448); and/or NVIAPGLESSCANSLLFVCLPVAHHRHNFLFIKHSLYNHLRDYESDFDKI (SEQ ID NO:449). Further embodiments of the invention are directed to polynucleotides which encode these polypeptides.

This gene is expressed primarily in T cells, fetal heart and infant brain and to a lesser extent in some transformed cell lines.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of growth and immune disorders and diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and cardiovascular systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., T-cells and other cells and tissue of the immune system, heart and vesicular tissue, brain and other tissue of the nervous system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for study and treatment of developmental and immune disorders. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:119 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or

more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1428 of SEQ ID NO:119, b is an integer of 15 to 1442, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:119, and where b is greater than or equal to a + 14.

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## FEATURES OF PROTEIN ENCODED BY GENE NO: 110

Additional embodiments of the invention are directed to polypeptides comprising the following amino acid sequences:  
 PKVLAVLKKKNHVALSIFELLSNDICSFISFFMS (SEQ ID NO:450); EGPDIN  
 SNLKFLLCLKKKIMWPFQYLNC (SEQ ID NO:451); and/or LLSLILLRIWYD  
 FSKQTVFWFFLNVFNFSSCNNDGACSYKYRKVQI (SEQ ID NO:452). Further  
 embodiments of the invention are directed to polynucleotides which encode these  
 polypeptides.

15

This gene is expressed primarily in osteoblasts and to a lesser extent in bone marrow and bladder.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, skeletal and hemopoietic diseases and disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the skeletal and vascular systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., bone, bone marrow, and bladder, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:259 as residues: Gly-33 to Lys-38.

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The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the study, diagnosis, and treatment of bone and hematopoietic disorders. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:120 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are

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specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 831 of SEQ ID NO:120, b  
5 is an integer of 15 to 845, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:120, and where b is greater than or equal to a + 14.

#### FEATURES OF PROTEIN ENCODED BY GENE NO: 111

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Additional embodiments of the invention are directed to polypeptides comprising the following amino acid sequences: HTLFISFLWAEG (SEQ ID NO:453); MLPVFVLFFCFTYSARKQSVFKKGNVFE (SEQ ID NO:454); and/or SPCSAA ECHNLSLLS SCSLVSSNILFSFPFFGQKARCCCLFLFYFSASHIAHESRVYSK  
15 KEMCL (SEQ ID NO:455). Further embodiments of the invention are directed to polynucleotides which encode these polypeptides.

This gene is expressed primarily in prostate cancer.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a  
20 biological sample and for diagnosis of diseases and conditions which include, but are not limited to, prostate and other cancers. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the endocrine system, expression of this gene  
25 at significantly higher or lower levels may be routinely detected in certain tissues (e.g., prostate, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the  
30 disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for study and treatment of prostate cancer and other neoplasias. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are  
35 related to SEQ ID NO:121 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.

Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 346 of SEQ ID NO:121, b is an integer of 15 to 360, where both a and b correspond to the positions of nucleotide residues shown in  
 5 SEQ ID NO:121, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 112

10 Additional embodiments of the invention are directed to polypeptides comprising the following amino acid sequences:  
 HKCFQCFLANGFLKVIKPFQRNWSDKTFFLVCLNKAISEALLSKMTFLSFFKT  
 NLLLLETFTCTI (SEQ ID NO:456); LLGVLPYFSVEPVLGERSVAFEVREKNH  
 GTSGFLSLYSLAAIVCGHLMFFHTLLGRGGNDHPGQSPLPGMRPLRGGL  
 15 AGQAPSGHPWMQPLDTCLL (SEQ ID NO:457); RPTRPPTRPDRPSLELAPG  
 LCADFLGSSNHCIFLLSLYLGRDQ (SEQ ID NO:458); and/or EKRIMVPQGF  
 FPFTRWQPLSVGTSCFSTLYWAVEVTITQASLLCLGCAL (SEQ ID NO:459).  
 Further embodiments of the invention are directed to polynucleotides which encode these polypeptides.

20 This gene is expressed primarily in haemopoietic and neural tissues and to a lesser extent in a number of cancers and other tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are  
 25 not limited to, diseases of the haemopoietic and neural systems. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and neural system, expression of this gene at significantly higher or lower levels may be routinely detected  
 30 in certain tissues (e.g., haematopoietic tissue, and neural cells and tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

35 The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of diseases of the haemopoietic and neural systems including several cancers. Many polynucleotide

sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:122 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 930 of SEQ ID NO:122, b is an integer of 15 to 944, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:122, and where b is greater than or equal to a + 14.

### FEATURES OF PROTEIN ENCODED BY GENE NO: 113

The translation product of this gene shares sequence homology with intestinal epithelium proliferating cell-associated mRNA sequence which is thought to be important in growth and development of epithelial cells. Additional embodiments of the invention are directed to polypeptides comprising the following amino acid sequences: MTLDEWKNLQEQTRPKPEFNIRKPESTVPSKAVVIRESKYRDDMVKDDYEDDS HVFRKPANDITSQLEINFGNLPRPGRGARGGTRGGRGRIRRAENYGPRAEVVM QDVAPNPDDPEDFPALS (SEQ ID NO:460); CKMLPPTQMTRKISLRCLERALFP STAELHCTPVGRLFQLGQGSQTLRTIDVAFPVSCKFVALFWAELLEGLL QRLESRPFPKKMKNKGDCVFIEGISNEE (SEQ ID NO:461); PPSSWAWS QRRHPGRPGKDQEGRELWTQSRSGDARCCPQPR (SEQ ID NO:462); and/or CLKCVYRDSIDSSAEAWRERRL (SEQ ID NO:463). Further embodiments of the invention are directed to polynucleotides which encode these polypeptides.

This gene is expressed primarily in brain and central nervous system and to a lesser extent in testis.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases of the neural system. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the neural and reproductive system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., brain and other cells and tissue of the nervous system, testis and other

reproductive tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:262 as residues: Glu-20 to Glu-27, Glu-30 to Trp-44.

The tissue distribution and homology to intestinal epithelium proliferating cell-associated mRNA sequence indicates that polynucleotides and polypeptides corresponding to this gene are useful for growth and developmental diseases of the brain, central nervous system and reproductive system. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:123 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 900 of SEQ ID NO:123, b is an integer of 15 to 914, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:123, and where b is greater than or equal to a + 14.

#### FEATURES OF PROTEIN ENCODED BY GENE NO: 114

Additional embodiments of the invention are directed to polypeptides comprising the following amino acid sequences: LSYSVLLILP LFHSLPTL KDTHTHNKWVE (SEQ ID NO:464); EVNGVGYKHSCFSDISSVLENKDS RMRAPHYASFQHFFSVLLKLSPQACLTESQCIPLTFY (SEQ ID NO:465); KTHHTISGWSKKSTELDISIP AFLTSPVSWRTRILE (SEQ ID NO:466); and/or IRHELGSSDPPAEASQIAGTAAVSHHAQP (SEQ ID NO:467). Further embodiments of the invention are directed to polynucleotides which encode these polypeptides.

This gene is expressed primarily in spinal cord.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, spinal cord injuries and diseases of the neural system. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing



immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the neural system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., spinal cord and other cells and tissue of the nervous system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:263 as residues: Pro-45 to Gln-52.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of spinal cord injuries and diseases of the neural system. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:124 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 448 of SEQ ID NO:124, b is an integer of 15 to 462, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:124, and where b is greater than or equal to a + 14.

## 25 FEATURES OF PROTEIN ENCODED BY GENE NO: 115

Additional embodiments of the invention are directed to polypeptides comprising the following amino acid sequences: MLYLILISLSSLSFSFSLPPFSIII (SEQ ID NO:468); SSYFLRHFRITYHTCPKYFSMNIN (SEQ ID NO:469); KLTLTGKNKSWSSSTAVAAALELVDPPGCRNSARDSLPNSTM MFYYAC FLYSSLSPLSLSLSPSLLSLL (SEQ ID NO:470); and/or QFHTGNSYDHDYAK (SEQ ID NO:471). Further embodiments of the invention are directed to polynucleotides which encode these polypeptides.

This gene is expressed primarily in striatum.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of a number of diseases of the neural system.

Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the neural diseases, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., striatum, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of diseases of the neural system. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:125 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 531 of SEQ ID NO:125, b is an integer of 15 to 545, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:125, and where b is greater than or equal to a + 14.

## FEATURES OF PROTEIN ENCODED BY GENE NO: 116

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Additional embodiments of the invention are directed to polypeptides comprising the following amino acid sequences:

AVCTGGGYCESCRCEHCVCVCVDLCVLFSGKELRVR (SEQ ID NO:472); VSFFV  
FKWSFAEIKSREEHWASLTPKPTLLSALLTCDVLKSSIIFKCESTEDKGFDSFF  
30 QASKDGSSSRI (SEQ ID NO:473); RSWGSRSLCLLPFAAESYSVWVMGHL  
FVVCLSSWWTFRPFALAVTVNHVAVNIVCVSAWTCVSCSLGRSCGLEGSFLF  
PLETLWFPHMVVLCLTF (SEQ ID NO:474); GHLFVVCLSSWWTFRPFALAVT  
VNHVAVNIVCVSAWTCVSCSLGRSCGLEGSFLFPLETLWFPHMVVLCLTF  
(SEQ ID NO:475); HDVLGARNACVCCSFLQQRILLFGWATCLLSVYSPA  
35 GGHLGR LHWRL (SEQ ID NO:476); MLDFKTSQVSKALKRVGFGVRLAQ  
CSSLDLISAKLHLKTKKKETYTTSTVMTAASLFLSYVTSEFTRSIMATFYCFVL  
KLHIGEMGTLQTAGGSKMTWPLQKAIWQFLKRLSIKLPYVETRESPGETKNY

(SEQ ID NO:477); and/or LTRNSFPENRTHKSTQTHTQCSQRHDSQ (SEQ ID NO:478). Further embodiments of the invention are directed to polynucleotides which encode these polypeptides.

This gene is expressed primarily in intestine and cancer cells.

5 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases of the gastrointestinal tract and cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological  
10 probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the digestive system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., gastrointestinal tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or  
15 cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment and diagnosis of diseases of the  
20 digestive system and cancer. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:126 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related  
25 sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 898 of SEQ ID NO:126, b is an integer of 15 to 912, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:126, and where b is greater than or equal to a + 14.

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#### FEATURES OF PROTEIN ENCODED BY GENE NO: 117

The translation product of this gene shares sequence homology with a human apoptosis regulating protein which is thought to be important in regulating cell death.

35 Additional embodiments of the invention are directed to polypeptides comprising the following amino acid sequences:

IRHEGQSSSRGSSHCDSPSPQEDGQIMFDVEMHTSRDHSSQSEEEVVEGEKEVE

ALKKSADWVSDWSSRPENIPPKEFHFRHPKRSVLS (SEQ ID NO:479);  
 GILLTLYPFWPEDILEFPNRYVCCLEICKGFFSANATSRL (SEQ ID NO:480);  
 EFGTRDRVVPEAVLTVTALRHKKMGRSCLMWKCTPAGTIALSQKKKL (SEQ  
 ID NO:481); AHPLPAPTEGKEKPLEMRVTCEVVYCHSSLFELETIVSMTQPTT  
 5 LFLHIQFQ (SEQ ID NO:482); TFCVFKHEEKWSHEERGYFLRRISEGVHSISLPF  
 SCFGFGARHLYWKATEHTLCQHLLRERKSPWKCV (SEQ ID NO:483); and/or  
 QSLLLFRNLQGLLFRKCHQQIILSAMLSSLISATRLDLYHSWYKFYSCNI  
 TTISLLKRDQVSK (SEQ ID NO:484). Further embodiments of the invention are  
 directed to polynucleotides which encode these polypeptides.

10 This gene is expressed primarily in muscle, fibroblast cells, haemopoietic cells,  
 fetal lung and to a lesser extent in several other tissues and cells.

Therefore, polynucleotides and polypeptides of the invention are useful as  
 reagents for differential identification of the tissue(s) or cell type(s) present in a  
 biological sample and for diagnosis of diseases and conditions which include, but are  
 15 not limited to, diseases of the haemopoietic, muscular and developing system.  
 Similarly, polypeptides and antibodies directed to these polypeptides are useful in  
 providing immunological probes for differential identification of the tissue(s) or cell  
 type(s). For a number of disorders of the above tissues or cells, particularly of the  
 immune and muscular system, expression of this gene at significantly higher or lower  
 20 levels may be routinely detected in certain tissues (e.g., muscle, fibroblast and other  
 cells and tissue of the nervous system, haemotopoietic cells, and lung, and cancerous  
 and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and  
 spinal fluid) or another tissue or cell sample taken from an individual having such a  
 disorder, relative to the standard gene expression level, i.e., the expression level in  
 25 healthy tissue or bodily fluid from an individual not having the disorder. Preferred  
 epitopes include those comprising a sequence shown in SEQ ID NO:266 as residues:  
 Met-1 to Ala-6.

The tissue distribution and homology to apoptosis regulating protein indicates  
 that polynucleotides and polypeptides corresponding to this gene are useful for  
 30 diagnosis and treatment of diseases of the haemopoietic, muscular and developing  
 system. Many polynucleotide sequences, such as EST sequences, are publicly available  
 and accessible through sequence databases. Some of these sequences are related to SEQ  
 ID NO:127 and may have been publicly available prior to conception of the present  
 invention. Preferably, such related polynucleotides are specifically excluded from the  
 35 scope of the present invention. To list every related sequence is cumbersome.  
 Accordingly, preferably excluded from the present invention are one or more  
 polynucleotides comprising a nucleotide sequence described by the general formula of

a-b, where a is any integer between 1 to 1034 of SEQ ID NO:127, b is an integer of 15 to 1048, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:127, and where b is greater than or equal to a + 14.

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## FEATURES OF PROTEIN ENCODED BY GENE NO: 118

Additional embodiments of the invention are directed to polypeptides comprising the following amino acid sequences: IRHEESFNPLTCGFSLFFSLFS  
 10 (SEQ ID NO:485); METLLLLLFFLSLLIFRFRILVSQCIN (SEQ ID NO:486);  
 FLLTTVLLFSSKVRDP RANFDQSLRVLKHAKKVQPDVISKTSIMLGLGEND  
 EQVYATMKGKEIEK (SEQ ID NO:487); and/or QQSCCFPVRFVILGPILISPYVY  
 (SEQ ID NO:488). Further embodiments of the invention are directed to  
 polynucleotides which encode these polypeptides.

15 This gene is expressed primarily in synovium.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, arthritis and other diseases of the musculo-skeletal system. Similarly,  
 20 polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the musculo-skeletal system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., synovial tissue, and cancerous and wounded tissues) or  
 25 bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides  
 30 corresponding to this gene are useful for treatment and diagnosis of diseases of the muscular-skeletal system. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:128 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically  
 35 excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general

formula of a-b, where a is any integer between 1 to 708 of SEQ ID NO:128, b is an integer of 15 to 722, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:128, and where b is greater than or equal to a + 14.

5

## FEATURES OF PROTEIN ENCODED BY GENE NO: 119

Additional embodiments of the invention are directed to polypeptides comprising the following amino acid sequences:

- 10 VWLLSSILLRVLWNRYTLQELSFWLPWFASRATSLVLQHGDNYLLFLFCFVCF  
VLAMPF (SEQ ID NO:489); IRHEVSMAFVFHFLAQGTLEPLYIAGA (SEQ ID  
NO:490); NSARGEYGFCLPSCSGYFGTAIHCRSLASGYHGLLPEQQA (SEQ ID  
NO:491); and/or HELTVPSRMGSKGKPYPCGFYSSLIP (SEQ ID NO:492). Further  
embodiments of the invention are directed to polynucleotides which encode these  
15 polypeptides.

This gene is expressed primarily in rejected kidney, stromal cells, and infant brain.

- Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a  
20 biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases of the renal, central nervous and immune systems. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune, renal and  
25 central nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., kidney, stromal cells, brain and other cells and tissue of the nervous system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard  
30 gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:268 as residues: Ser-6 to Arg-15.

- The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of diseases of the  
35 renal, central nervous, and immune systems. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:129 and may have been publicly

available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence  
 5 described by the general formula of a-b, where a is any integer between 1 to 463 of SEQ ID NO:129, b is an integer of 15 to 477, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:129, and where b is greater than or equal to a + 14.

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### FEATURES OF PROTEIN ENCODED BY GENE NO: 120

The protein of the invention has sequence identity to the *Saccharomyces cerevisiae* ankyrin repeat-containing protein (gil466522). Additional embodiments of the  
 15 invention are directed to polypeptides comprising the following amino acid sequences: KCIYPKPARTHHCSICNRCVLKMDHHCPWLNNCVGHYNHRYFFSFCFFMTLG CVYCSYGSWDLFREAYAAIEKMKQLDKNKLQAVANQTYHQTPPPTFSFRER (SEQ ID NO: 493); ARGHWNLILIVFHYYQAITPPGYPPQGRNDIATVSIC (SEQ ID NO:494); WQCELCVSHDSSTHSAPYVISRASKGSFSQNP (SEQ ID NO:495);  
 20 SKRASGPALGYHAGQFKDQPFYHCRRTQCGEILGLTSLYSGKQKFQPPQTR GQAASYLPCPVLTRTSSRIQHWSWPPPLLLAV (SEQ ID NO:496); ESLQLRLLGQ LEGIPGCGYRKALAYSGALTF (SEQ ID NO:497); and/or SLAPWEWNELGA PSLGDCSLSLCDGSVSWTVSATRALILLPMLFQGPPRAAFLRILDQKEPVGLP (SEQ ID NO:498). Further embodiments of the invention are directed to  
 25 polynucleotides which encode these polypeptides.

This gene is expressed primarily in endometrial tumor and to a lesser extent in several other tissues and organs.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a  
 30 biological sample and for diagnosis of a number of types of cancers, particularly endometrial cancers. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the endometrium, expression of this gene at significantly higher or lower  
 35 levels may be routinely detected in certain tissues (e.g., endometrium and other reproductive tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken

from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:269 as residues: Asn-43 to Arg-49, Phe-57 to Cys-65, Pro-93 to Ser-99.

- 5           The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of diseases and cancers of the endometrium and cancers of several different organs and tissue. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:130
- 10           and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is
- 15           any integer between 1 to 1282 of SEQ ID NO:130, b is an integer of 15 to 1296, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:130, and where b is greater than or equal to a + 14.

## 20    **FEATURES OF PROTEIN ENCODED BY GENE NO: 121**

The translation product of this gene shares sequence homology with adrenalin receptor. Additional embodiments of the invention are directed to polypeptides comprising the following amino acid sequences:

- 25    TATLNSFFGGWGLALLLRLECSDTIMDHCSLDLLGSSNPPASASQVVGTTGAR  
HHAQLIFCFFVQTRSHSVA (SEQ ID NO:499); MDHCSLDLLGSSNPPASASQV  
VGTTGARHHAQLIFCFFVQTRSHSVA (SEQ ID NO:500); GVLKQSSHLVLSKG  
(SEQ ID NO:501); DYSCESLCPALLSIAPDIVLN (SEQ ID NO:502); TTIHKTQLGS  
YKILWEPKEGYHNSTWI (SEQ ID NO:503); IREIFLRRP (SEQ ID NO:504); and/or
- 30    LKFQKPGKIQMRGGGRVFWYKNCK (SEQ ID NO:505). Further embodiments of the invention are directed to polynucleotides which encode these polypeptides.

This gene is expressed primarily in synovial sarcoma.

- Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a
- 35    biological sample and for diagnosis of diseases and conditions which include, but are not limited to, arthritis and other diseases of the synovium including cancers. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing



immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and muscular-skeletal system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., synovial tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology to adrenalin receptor indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of diseases of the synovium, immune system and musculo-skeletal system including cancers of these tissues and systems. It may also be useful for identifying and therapeutically using antagonists and agonists for this receptor family. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:131 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 724 of SEQ ID NO:131, b is an integer of 15 to 738, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:131, and where b is greater than or equal to a + 14.

25

#### **FEATURES OF PROTEIN ENCODED BY GENE NO: 122**

Additional embodiments of the invention are directed to polypeptides comprising the following amino acid sequences:

30 NSARVTQKGESVGSVGC MRAIAGFDNYPLF (SEQ ID NO:506);  
 GTIGIFWPLPVAILSSGDYLQTQIHRPLLHRGT (SEQ ID NO:507);  
 LPLPLSSLLHIATCNPFPKT (SEQ ID NO:508);  
 SYFFVYNLILKIIQGDHASIILLATIPIFGDIYYVKGQLASFGPYL (SEQ ID  
 NO:509); LFYHLEIISRHKSHCSIEA (SEQ ID NO:510); CSCHCPSRAFST (SEQ  
 35 ID NO:511); and/or PHAIHSQKPSSIFLITDVFPDPPVGIYLL (SEQ ID NO:512).  
 Further embodiments of the invention are directed to polynucleotides which encode these polypeptides.

This gene is expressed primarily in chronic synovitis. .

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, inflammatory diseases and disorders of the musculo-skeletal system. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the inflammatory and musculo-skeletal system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues (e.g., synovial tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO:271 as residues: Ser-39 to Pro-44.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment and diagnosis of disorders and diseases of the inflammatory and musculo-skeletal system. Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:132 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 428 of SEQ ID NO:132, b is an integer of 15 to 442, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:132, and where b is greater than or equal to a + 14.

30

### FEATURES OF PROTEIN ENCODED BY GENE NO: 123

Additional embodiments of the invention are directed to polypeptides comprising the following amino acid sequences:  
 RKL FHKINSKSFHLSGMHILISVWIVRSRIKVKYELLLCFFDVIFYV (SEQ ID NO:513); NSARDVFFTQKILYSQTCIFFPCLVPFSFLFSFFFFLSFVG (SEQ ID

35

NO:514); MFSSLKKFYILKHVYSFPVLFHFLFFFLFSFSFLSWAEKGAGKMKLA  
TENCKMVKS (SEQ ID NO:515); and/or

IQLLYLKGAAMKYLSYVARLLFLKALDLF APKMVQIDSF (SEQ ID NO:516).

Further embodiments of the invention are directed to polynucleotides which encode  
5 these polypeptides.

This gene is expressed primarily in kidney and infant brain and to a lesser extent  
in several other tissues and organs.

Therefore, polynucleotides and polypeptides of the invention are useful as  
reagents for differential identification of the tissue(s) or cell type(s) present in a  
10 biological sample and for diagnosis of diseases and conditions which include, but are  
not limited to, diseases of the renal and central nervous systems. Similarly,  
polypeptides and antibodies directed to these polypeptides are useful in providing  
immunological probes for differential identification of the tissue(s) or cell type(s). For a  
number of disorders of the above tissues or cells, particularly of the neural and renal  
15 system, expression of this gene at significantly higher or lower levels may be routinely  
detected in certain tissues (e.g., renal tissue, and brain and other cells and tissue of the  
nervous system, and cancerous and wounded tissues) or bodily fluids (e.g., serum,  
plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken  
from an individual having such a disorder, relative to the standard gene expression  
20 level, i.e., the expression level in healthy tissue or bodily fluid from an individual not  
having the disorder. Preferred epitopes include those comprising a sequence shown in  
SEQ ID NO:272 as residues: Gly-24 to Lys-31.

The tissue distribution indicates that polynucleotides and polypeptides  
corresponding to this gene are useful for diagnosis and treatment of diseases of the  
25 neural and renal systems. Many polynucleotide sequences, such as EST sequences, are  
publicly available and accessible through sequence databases. Some of these sequences  
are related to SEQ ID NO:133 and may have been publicly available prior to conception  
of the present invention. Preferably, such related polynucleotides are specifically  
excluded from the scope of the present invention. To list every related sequence is  
30 cumbersome. Accordingly, preferably excluded from the present invention are one or  
more polynucleotides comprising a nucleotide sequence described by the general  
formula of a-b, where a is any integer between 1 to 868 of SEQ ID NO:133, b is an  
integer of 15 to 882, where both a and b correspond to the positions of nucleotide  
residues shown in SEQ ID NO:133, and where b is greater than or equal to a + 14.

35 —

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
1	HCEIA77	209119 06/12/97	Uni-ZAP XR	11	1882	676	1882	785	785	150	1	37	38	53
2	HCFCE10	209119 06/12/97	pSport1	12	1590	18	1590	198	198	151	1	19	20	45
3	HCFNC26	209119 06/12/97	pSport1	13	1373	6	1373	85	85	152	1	18	19	24
4	HCHAA63	209119 06/12/97	pSport1	14	1142	1	1142	130	130	153	1	37	38	264
5	HCNSP40	209119 06/12/97	pBluescript	15	1034	1	1034	106	106	154	1	19	20	237
5	HCNSP40	209119 06/12/97	pBluescript	134	1032	1	1032		111	273	1			14
6	HDAAC10	209119 06/12/97	pSport1	16	1198	1	1198	117	117	155	1	21	22	313
7	HE8CV18	209119 06/12/97	Uni-ZAP XR	17	1447	1	1447	176	176	156	1	29	30	98
8	HELDY05	209119 06/12/97	Uni-ZAP XR	18	1422	1	1375	79	79	157	1	34	35	36
9	HELDZ32	209119 06/12/97	Uni-ZAP XR	19	1107	12	1107	148	148	158	1	15	16	22
10	HFGAL10	209119 06/12/97	Uni-ZAP XR	20	1183	1	1183	179	179	159	1	20	21	96
10	HFGAL10	209119 06/12/97	Uni-ZAP XR	135	1766	3	1765	179	179	274	1	17	18	36
11	HFKEB72	209119 06/12/97	Uni-ZAP XR	21	1420	1	1420	43	43	160	1	29	30	65

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
12	HFTCU19	209119 06/12/97	Uni-ZAP XR	22	1575	1266	1575	137	137	161	1	30	31	222
12	HFTCU19	209119 06/12/97	Uni-ZAP XR	136	470	1	470	157	157	275	1	24	25	56
13	HFXHN31	209119 06/12/97	Lambda ZAP II	23	541	1	541	172	172	162	1	30	31	91
13	HFXHN31	209119 06/12/97	Lambda ZAP II	137	1168	1	1168	293	293	276	1	22	23	26
14	HGLAM53	209119 06/12/97	Uni-ZAP XR	24	833	219	833	359	359	163	1	27	28	74
14	HGLAM53	209119 06/12/97	Uni-ZAP XR	138	1294	226	1288		369	277	1	26	27	67
15	HJABB94	209119 06/12/97	pBluescript SK-	25	1555	1	1555	74	74	164	1	28	29	77
16	HKIYO61	209119 06/12/97	pBluescript	26	1543	1	1543	181	181	165	1	19	20	37
17	HLTAI94	209119 06/12/97	Uni-ZAP XR	27	1262	1	1262	47	47	166	1	18	19	44
18	HMDAI51	209119 06/12/97	Uni-ZAP XR	28	753	1	753	12	12	167	1	21	22	38
19	HMELR03	209119 06/12/97	Lambda ZAP II	29	1621	8	1535	200	200	168	1	25	26	173
20	HMKAH10	209119 06/12/97	pSport1	30	921	1	921	48	48	169	1	43	44	54
21	HMKCW19	209119 06/12/97	pSport1	31	2095	473	1934	529	529	170	1	30	31	344

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
21	HMKCW19	209119 06/12/97	pSport1	139	1720	103	1692	188	188	278	1	27	28	45
22	HMSJW18	209119 06/12/97	Uni-ZAP XR	32	1838	1	1838	28	28	171	1	23	24	89
23	HMWGY01	209119 06/12/97	Uni-Zap XR	33	782	1	782	423	423	172	1	30	31	104
23	HMWGY01	209119 06/12/97	Uni-Zap XR	140	774	1	774	17	17	279	1	31	32	39
24	HNFID82	209119 06/12/97	pBluescript	34	1560	1	1560	161	161	173	1	17	18	41
25	HNFIG36	209119 06/12/97	pBluescript	35	1092	1	1082	171	171	174	1	18	19	46
26	HNGEV29	209119 06/12/97	Uni-ZAP XR	36	1153	1	1153	173	173	175	1	30	31	73
26	HNGEV29	209119 06/12/97	Uni-ZAP XR	141	1566	1	1566	79	79	280	1			10
27	HNGIK21	209119 06/12/97	Uni-ZAP XR	37	985	1	985	152	152	176	1	25	26	28
28	HNGJJ65	209124 06/19/97	Uni-ZAP XR	38	1122	1	1122	84	84	177	1	22	23	67
29	HNGJU42	209124 06/19/97	Uni-ZAP XR	39	598	6	598	273	273	178	1	17	18	23
30	HODAZ26	209124 06/19/97	Uni-ZAP XR	40	1129	8	1129	133	133	179	1			30
31	HODDB05	209124 06/19/97	Uni-ZAP XR	41	1158	22	1158	244	244	180	1			10

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA ORF
32	HOF39	209124 06/19/97	pSport1	42	1767	1	1767	57	57	181	1	22	23	31
33	HOF71	209124 06/19/97	pCMVSPORT 2.0	43	917	1	917	114	114	182	1	31	32	35
34	HOB81	209124 06/19/97	Uni-ZAP XR	44	1987	8	1965	31	31	183	1	34	35	34
35	HOCY73	209124 06/19/97	Uni-ZAP XR	45	2053	196	2048	209	209	184	1			28
36	HPMBR15	209124 06/19/97	Uni-ZAP XR	46	1272	25	1272	262	262	185	1			5
37	HSVVD46	209124 06/19/97	Uni-ZAP XR	47	773	2	767		173	186	1	21	22	52
38	HSLBF69	209124 06/19/97	Uni-ZAP XR	48	2119	1	2119	107	107	187	1	19	20	405
39	HSOAH66	209124 06/19/97	Uni-ZAP XR	49	1188	7	1188	196	196	188	1	27	28	36
39	HSOAH66	209124 06/19/97	Uni-ZAP XR	143	537	1	537	136	136	282	1	21	22	47
40	HSVBH58	209124 06/19/97	Uni-ZAP XR	50	478	24	155	249	249	189	1	40	41	57
40	HSVBH58	209124 06/19/97	Uni-ZAP XR	144	680	1	680	168	168	283	1	20	21	22
41	HSZAF47	209124 06/19/97	Uni-ZAP XR	51	1333	2	1333	107	107	190	1	18	19	126
42	HTADV27	209124 06/19/97	Uni-ZAP XR	52	1255	14	1255	69	69	191	1	20	21	20

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
43	HTADX17	209124 06/19/97	Uni-ZAP XR	53	1140	22	1140	84	84	192	1	24	25	142
44	HTDAD22	209124 06/19/97	pSport1	54	1220	1	1220	193	193	193	1	37	38	109
45	HTEDS39	209124 06/19/97	Uni-ZAP XR	55	694	198	694	205	205	194	1	21	22	80
45	HTEDS39	209124 06/19/97	Uni-ZAP XR	145	1048	1	1048		227	284	1			20
46	HTEHH53	209124 06/19/97	Uni-ZAP XR	56	988	1	980	22	22	195	1	24	25	209
47	HTLDP69	209124 06/19/97	Uni-ZAP XR	57	1500	237	1500	330	330	196	1	29	30	148
48	HTNBR95	209124 06/19/97	pBluescript SK-	58	1391	1	1386	70	70	197	1	28	29	35
49	HTPCS60	209124 06/19/97	Uni-ZAP XR	59	1579	7	1259	105	105	198	1	19	20	257
50	HUKBH05	209124 06/19/97	Lambda ZAP II	60	1241	1	1215	151	151	199	1	18	19	58
51	HUKEX85	209124 06/19/97	Lambda ZAP II	61	930	7	925	35	35	200	1	18	19	33
51	HUKEX85	209124 06/19/97	Lambda ZAP II	146	930	6	917	83	83	285	1	30	31	122
52	HWTBM45	209124 06/19/97	Uni-ZAP XR	62	998	1	998	69	69	201	1	19	20	25
53	HADFF38	209124 06/19/97	pSport1	63	1193	1	1034	64	64	202	1	19	20	33



Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
54	HADFK68	209124 06/19/97	pSport1	64	830	1	830	91	91	203	1	24	25	58
54	HADFK68	209124 06/19/97	pSport1	147	830	1	830	45	45	286	1	26	27	26
55	HADGG19	209125 06/19/97	pSport1	65	867	1	867	262	262	204	1	30	31	75
55	HADGG19	209125 06/19/97	pSport1	148	865	1	865	281	281	287	1			7
56	HAEAV45	209125 06/19/97	pBluescript SK-	66	685	46	647	487	487	205	1	34	35	66
56	HAEAV45	209125 06/19/97	pBluescript SK-	149	545	1	545	24	24	288	1	25	26	28
57	HARAA15	209125 06/19/97	pBluescript SK-	67	801	1	801	185	185	206	1	34	35	43
58	HATDL27	209125 06/19/97	Uni-ZAP XR	68	908	1	908	82	82	207	1	28	29	31
59	HBAFQ54	209125 06/19/97	pSport1	69	696	209	696	229	229	208	1	20	21	47
60	HGBA14	209125 06/19/97	Uni-ZAP XR	70	455	1	452	32	32	209	1	24	25	36
61	HBIAS26	209125 06/19/97	Uni-ZAP XR	71	413	1	372	57	57	210	1	27	28	73
62	HBJFU48	209125 06/19/97	Uni-ZAP XR	72	849	1	849	20	20	211	1	39	40	40
63	HBJFV28	209125 06/19/97	Uni-ZAP XR	73	505	1	505	306	306	212	1	21	22	53

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
64	HBMWB01	209125 06/19/97	Uni-ZAP XR	74	719	1	719	48	48	213	1	17	18	62
65	HBMXN79	209125 06/19/97	Uni-ZAP XR	75	1274	141	974	192	192	214	1	44	45	175
66	HBMXP84	209125 06/19/97	Uni-ZAP XR	76	519	1	519	161	161	215	1	31	32	39
67	HCFMM26	209125 06/19/97	pSport1	77	389	1	389	178	178	216	1	27	28	54
68	HCNAV36	209125 06/19/97	Lambda ZAP II	78	823	411	823	505	505	217	1	15	16	46
69	HCNSB01	209125 06/19/97	pBluescript	79	2455	533	1308	552	552	218	1	22	23	179
70	HCRBR74	209125 06/19/97	Uni-ZAP XR	80	921	365	911	415	415	219	1	20	21	98
71	HCUBN59	209125 06/19/97	ZAP Express	81	678	1	678	96	96	220	1	39	40	43
72	HCUDB38	209125 06/19/97	ZAP Express	82	857	1	857	221	221	221	1	17	18	41
73	HCUFZ62	209125 06/19/97	ZAP Express	83	1977	28	661	233	233	222	1	28	29	51
74	HDHMB42	209125 06/19/97	pCMVSPORT 2.0	84	1149	427	1149	592	592	223	1	26	27	31
75	HDPCO25	209125 06/19/97	pCMVSPORT 3.0	85	767	76	767	182	182	224	1	20	21	53
76	HDPHI51	209125 06/19/97	pCMVSPORT 3.0	86	728	1	728	245	245	225	1	30	31	40

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
77	HE2EC79	209125 06/19/97	Uni-ZAP XR	87	735	1	735	151	151	226	1	21	22	30
78	HE9FE83	209125 06/19/97	Uni-ZAP XR	88	889	332	889	351	351	227	1	21	22	59
79	HE9HW52	209125 06/19/97	Uni-ZAP XR	89	569	73	569	122	122	228	1	25	26	34
80	HEBFL88	209125 06/19/97	Uni-ZAP XR	90	334	2	334	76	76	229	1	22	23	38
81	HFIVB57	209125 06/19/97	pSport1	91	795	92	795	286	286	230	1	35	36	38
82	HFPDE69	209125 06/19/97	Uni-ZAP XR	92	577	1	577	72	72	231	1	33	34	61
83	HGBGV89	209125 06/19/97	Uni-ZAP XR	93	968	1	968	55	55	232	1	26	27	197
84	HGLDE38	209125 06/19/97	Uni-ZAP XR	94	553	1	553	31	31	233	1	19	20	61
85	HHGDU58	209125 06/19/97	Lambda ZAP II	95	968	70	898	235	235	234	1	46	47	80
86	HHTLF25	209125 06/19/97	ZAP Express	96	697	1	661	142	142	235	1	26	27	111
87	HJMAV91	209125 06/19/97	pCMVSPORT 3.0	97	866	74	866	251	251	236	1	16	17	32
88	HKAFB88	209125 06/19/97	pCMVSPORT 2.0	98	1368	219	795	238	238	237	1	45	46	228
89	HLHFP03	209126 06/19/97	Uni-ZAP XR	99	613	1	613	224	224	238	1	20	21	116

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
90	HLNAB07	209126 06/19/97	Lambda ZAP II	100	685	1	685	187	187	239	1	32	33	36
91	HLWCF05	209126 06/19/97	pCMVSPORT 3.0	101	646	1	646		159	240	1	20	21	38
92	HLYAF80	209126 06/19/97	pSport1	102	826	1	826	222	222	241	1	24	25	47
93	HMDAA66	209126 06/19/97	Uni-ZAP XR	103	586	1	586	106	106	242	1	23	24	31
94	HMKDD07	209126 06/19/97	pSport1	104	628	43	628	267	267	243	1	29	30	63
95	HMKDS08	209126 06/19/97	pSport1	105	558	1	558	230	230	244	1	30	31	67
96	HMSHM14	209126 06/19/97	Uni-ZAP XR	106	756	1	756	103	103	245	1	29	30	45
97	HMWDC28	209126 06/19/97	Uni-Zap XR	107	1146	105	754	124	124	246	1	30	31	42
98	HNDH54	209126 06/19/97	pCMVSPORT 2.0	108	775	1	775	26	26	247	1	20	21	31
99	HNFD53	209126 06/19/97	Uni-ZAP XR	109	911	1	911	200	200	248	1	22	23	23
100	HNFIU96	209126 06/19/97	pBluescript	110	456	1	456	170	170	249	1	33	34	79
101	HNGAC63	209126 06/19/97	Uni-ZAP XR	111	554	1	554	214	214	250	1			15
102	HNGAX58	209126 06/19/97	Uni-ZAP XR	112	722	1	722	100	100	251	1	16	17	46

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
103	HNGEM24	209126 06/19/97	Uni-ZAP XR	113	931	1	931	239	239	252	1	30	31	31
104	HNGFT78	209126 06/19/97	Uni-ZAP XR	114	588	1	588	20	20	253	1	29	30	35
105	HNHDL85	209126 06/19/97	Uni-ZAP XR	115	812	1	812	194	194	254	1	22	23	50
106	HNHFU59	209126 06/19/97	Uni-ZAP XR	116	506	1	506	278	278	255	1	16	17	76
107	HNHFW22	209126 06/19/97	Uni-ZAP XR	117	751	1	751	228	228	256	1	26	27	60
108	HOAAF80	209126 06/19/97	Uni-ZAP XR	118	960	131	960	303	303	257	1	33	34	36
109	HODCJ90	209126 06/19/97	Uni-ZAP XR	119	1442	326	1133	344	344	258	1	18	19	42
110	HOECO90	209126 06/19/97	Uni-ZAP XR	120	845	215	845	299	299	259	1	24	25	38
111	HPEBT80	209126 06/19/97	Uni-ZAP XR	121	360	1	360	21	21	260	1	40	41	50
112	HSDAG05	209126 06/19/97	Uni-ZAP XR	122	944	231	848	419	419	261	1	37	38	75
113	HSDGR57	209126 06/19/97	Uni-ZAP XR	123	914	115	914	195	195	262	1	21	22	44
114	HSDIJ82	209126 06/19/97	Uni-ZAP XR	124	462	1	462	79	79	263	1	32	33	52
115	HSDZM95	209126 06/19/97	pBluescript	125	545	1	545	223	223	264	1	23	24	42

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
116	HSID115	209126 06/19/97	Uni-ZAP XR	126	912	1	873		173	265	1	23	24	49
117	HSKYU29	209126 06/19/97	pBluescript	127	1048	1	1047	290	290	266	1	36	37	51
118	HSNAA55	209126 06/19/97	Uni-ZAP XR	128	722	1	722	35	35	267	1	15	16	40
119	HSQFP66	209126 06/19/97	Uni-ZAP XR	129	477	1	477	96	96	268	1	32	33	78
120	HSRDE35	209126 06/19/97	Uni-ZAP XR	130	1296	232	804	428	428	269	1	21	22	116
121	HSSJN64	209126 06/19/97	Uni-ZAP XR	131	738	1	738	70	70	270	1	33	34	61
122	HSVAQ28	209126 06/19/97	Uni-ZAP XR	132	442	1	442	149	149	271	1	24	25	98
123	HSVAY16	209126 06/19/97	Uni-ZAP XR	133	882	1	790	52	52	272	1	30	31	31

Table 1 summarizes the information corresponding to each "Gene No." described above. The nucleotide sequence identified as "NT SEQ ID NO:X" was assembled from partially homologous ("overlapping") sequences obtained from the "cDNA clone ID" identified in Table 1 and, in some cases, from additional related DNA clones. The overlapping sequences were assembled into a single contiguous sequence of high redundancy (usually three to five overlapping sequences at each nucleotide position), resulting in a final sequence identified as SEQ ID NO:X.

The cDNA Clone ID was deposited on the date and given the corresponding deposit number listed in "ATCC Deposit No:Z and Date." Some of the deposits contain multiple different clones corresponding to the same gene. "Vector" refers to the type of vector contained in the cDNA Clone ID.

"Total NT Seq." refers to the total number of nucleotides in the contig identified by "Gene No." The deposited clone may contain all or most of these sequences, reflected by the nucleotide position indicated as "5' NT of Clone Seq." and the "3' NT of Clone Seq." of SEQ ID NO:X. The nucleotide position of SEQ ID NO:X of the putative start codon (methionine) is identified as "5' NT of Start Codon." Similarly, the nucleotide position of SEQ ID NO:X of the predicted signal sequence is identified as "5' NT of First AA of Signal Pep."

The translated amino acid sequence, beginning with the methionine, is identified as "AA SEQ ID NO:Y," although other reading frames can also be easily translated using known molecular biology techniques. The polypeptides produced by these alternative open reading frames are specifically contemplated by the present invention.

The first and last amino acid position of SEQ ID NO:Y of the predicted signal peptide is identified as "First AA of Sig Pep" and "Last AA of Sig Pep." The predicted first amino acid position of SEQ ID NO:Y of the secreted portion is identified as "Predicted First AA of Secreted Portion." Finally, the amino acid position of SEQ ID NO:Y of the last amino acid in the open reading frame is identified as "Last AA of ORF."

SEQ ID NO:X and the translated SEQ ID NO:Y are sufficiently accurate and otherwise suitable for a variety of uses well known in the art and described further below. For instance, SEQ ID NO:X is useful for designing nucleic acid hybridization probes that will detect nucleic acid sequences contained in SEQ ID NO:X or the cDNA contained in the deposited clone. These probes will also hybridize to nucleic acid molecules in biological samples, thereby enabling a variety of forensic and diagnostic methods of the invention. Similarly, polypeptides identified from SEQ ID NO:Y may be used to generate antibodies which bind specifically to the secreted proteins encoded by the cDNA clones identified in Table 1.

Nevertheless, DNA sequences generated by sequencing reactions can contain sequencing errors. The errors exist as misidentified nucleotides, or as insertions or deletions of nucleotides in the generated DNA sequence. The erroneously inserted or deleted nucleotides cause frame shifts in the reading frames of the predicted amino acid sequence. In these cases, the predicted amino acid sequence diverges from the actual amino acid sequence, even though the generated DNA sequence may be greater than 99.9% identical to the actual DNA sequence (for example, one base insertion or deletion in an open reading frame of over 1000 bases).

Accordingly, for those applications requiring precision in the nucleotide sequence or the amino acid sequence, the present invention provides not only the generated nucleotide sequence identified as SEQ ID NO:X and the predicted translated amino acid sequence identified as SEQ ID NO:Y, but also a sample of plasmid DNA containing a human cDNA of the invention deposited with the ATCC, as set forth in Table 1. The nucleotide sequence of each deposited clone can readily be determined by sequencing the deposited clone in accordance with known methods. The predicted amino acid sequence can then be verified from such deposits. Moreover, the amino acid sequence of the protein encoded by a particular clone can also be directly determined by peptide sequencing or by expressing the protein in a suitable host cell containing the deposited human cDNA, collecting the protein, and determining its sequence.

The present invention also relates to the genes corresponding to SEQ ID NO:X, SEQ ID NO:Y, or the deposited clone. The corresponding gene can be isolated in accordance with known methods using the sequence information disclosed herein. Such methods include preparing probes or primers from the disclosed sequence and identifying or amplifying the corresponding gene from appropriate sources of genomic material.

Also provided in the present invention are species homologs. Species homologs may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source for the desired homologue.

The polypeptides of the invention can be prepared in any suitable manner. Such polypeptides include isolated naturally occurring polypeptides, recombinantly produced polypeptides, synthetically produced polypeptides, or polypeptides produced by a combination of these methods. Means for preparing such polypeptides are well understood in the art.

The polypeptides may be in the form of the secreted protein, including the mature form, or may be a part of a larger protein, such as a fusion protein (see below).



It is often advantageous to include an additional amino acid sequence which contains secretory or leader sequences, pro-sequences, sequences which aid in purification, such as multiple histidine residues, or an additional sequence for stability during recombinant production.

- 5           The polypeptides of the present invention are preferably provided in an isolated form, and preferably are substantially purified. A recombinantly produced version of a polypeptide, including the secreted polypeptide, can be substantially purified by the one-step method described in Smith and Johnson, *Gene* 67:31-40 (1988). Polypeptides of the invention also can be purified from natural or recombinant sources  
10       using antibodies of the invention raised against the secreted protein in methods which are well known in the art.

### Signal Sequences

- Methods for predicting whether a protein has a signal sequence, as well as the  
15       cleavage point for that sequence, are available. For instance, the method of McGeoch, *Virus Res.* 3:271-286 (1985), uses the information from a short N-terminal charged region and a subsequent uncharged region of the complete (uncleaved) protein. The method of von Heinje, *Nucleic Acids Res.* 14:4683-4690 (1986) uses the information from the residues surrounding the cleavage site, typically residues -13 to +2, where +1  
20       indicates the amino terminus of the secreted protein. The accuracy of predicting the cleavage points of known mammalian secretory proteins for each of these methods is in the range of 75-80%. (von Heinje, *supra*.) However, the two methods do not always produce the same predicted cleavage point(s) for a given protein.

- In the present case, the deduced amino acid sequence of the secreted polypeptide  
25       was analyzed by a computer program called SignalP (Henrik Nielsen et al., *Protein Engineering* 10:1-6 (1997)), which predicts the cellular location of a protein based on the amino acid sequence. As part of this computational prediction of localization, the methods of McGeoch and von Heinje are incorporated. The analysis of the amino acid sequences of the secreted proteins described herein by this program provided the results  
30       shown in Table 1.

- As one of ordinary skill would appreciate, however, cleavage sites sometimes vary from organism to organism and cannot be predicted with absolute certainty. Accordingly, the present invention provides secreted polypeptides having a sequence shown in SEQ ID NO:Y which have an N-terminus beginning within 5 residues (i.e., +  
35       or - 5 residues) of the predicted cleavage point. Similarly, it is also recognized that in some cases, cleavage of the signal sequence from a secreted protein is not entirely

uniform, resulting in more than one secreted species. These polypeptides, and the polynucleotides encoding such polypeptides, are contemplated by the present invention.

Moreover, the signal sequence identified by the above analysis may not necessarily predict the naturally occurring signal sequence. For example, the naturally occurring signal sequence may be further upstream from the predicted signal sequence. However, it is likely that the predicted signal sequence will be capable of directing the secreted protein to the ER. These polypeptides, and the polynucleotides encoding such polypeptides, are contemplated by the present invention.

#### 10 Polynucleotide and Polypeptide Variants

"Variant" refers to a polynucleotide or polypeptide differing from the polynucleotide or polypeptide of the present invention, but retaining essential properties thereof. Generally, variants are overall closely similar, and, in many regions, identical to the polynucleotide or polypeptide of the present invention.

By a polynucleotide having a nucleotide sequence at least, for example, 95% "identical" to a reference nucleotide sequence of the present invention, it is intended that the nucleotide sequence of the polynucleotide is identical to the reference sequence except that the polynucleotide sequence may include up to five point mutations per each 100 nucleotides of the reference nucleotide sequence encoding the polypeptide. In other words, to obtain a polynucleotide having a nucleotide sequence at least 95% identical to a reference nucleotide sequence, up to 5% of the nucleotides in the reference sequence may be deleted or substituted with another nucleotide, or a number of nucleotides up to 5% of the total nucleotides in the reference sequence may be inserted into the reference sequence. The query sequence may be an entire sequence shown in Table 1, the ORF (open reading frame), or any fragment specified as described herein.

As a practical matter, whether any particular nucleic acid molecule or polypeptide is at least 90%, 95%, 96%, 97%, 98% or 99% identical to a nucleotide sequence of the present invention can be determined conventionally using known computer programs. A preferred method for determining the best overall match between a query sequence (a sequence of the present invention) and a subject sequence, also referred to as a global sequence alignment, can be determined using the FASTDB computer program based on the algorithm of Brutlag et al. (Comp. App. Biosci. (1990) 6:237-245). In a sequence alignment the query and subject sequences are both DNA sequences. An RNA sequence can be compared by converting U's to T's. The result of said global sequence alignment is in percent identity. Preferred parameters used in a FASTDB alignment of DNA sequences to calculate percent identity are: Matrix=Unitary, k-tuple=4, Mismatch Penalty=1, Joining Penalty=30, Randomization

Group Length=0, Cutoff Score=1, Gap Penalty=5, Gap Size Penalty 0.05, Window Size=500 or the length of the subject nucleotide sequence, whichever is shorter.

If the subject sequence is shorter than the query sequence because of 5' or 3' deletions, not because of internal deletions, a manual correction must be made to the results. This is because the FASTDB program does not account for 5' and 3' truncations of the subject sequence when calculating percent identity. For subject sequences truncated at the 5' or 3' ends, relative to the query sequence, the percent identity is corrected by calculating the number of bases of the query sequence that are 5' and 3' of the subject sequence, which are not matched/aligned, as a percent of the total bases of the query sequence. Whether a nucleotide is matched/aligned is determined by results of the FASTDB sequence alignment. This percentage is then subtracted from the percent identity, calculated by the above FASTDB program using the specified parameters, to arrive at a final percent identity score. This corrected score is what is used for the purposes of the present invention. Only bases outside the 5' and 3' bases of the subject sequence, as displayed by the FASTDB alignment, which are not matched/aligned with the query sequence, are calculated for the purposes of manually adjusting the percent identity score.

For example, a 90 base subject sequence is aligned to a 100 base query sequence to determine percent identity. The deletions occur at the 5' end of the subject sequence and therefore, the FASTDB alignment does not show a matched/alignment of the first 10 bases at 5' end. The 10 unpaired bases represent 10% of the sequence (number of bases at the 5' and 3' ends not matched/total number of bases in the query sequence) so 10% is subtracted from the percent identity score calculated by the FASTDB program. If the remaining 90 bases were perfectly matched the final percent identity would be 90%. In another example, a 90 base subject sequence is compared with a 100 base query sequence. This time the deletions are internal deletions so that there are no bases on the 5' or 3' of the subject sequence which are not matched/aligned with the query. In this case the percent identity calculated by FASTDB is not manually corrected. Once again, only bases 5' and 3' of the subject sequence which are not matched/aligned with the query sequence are manually corrected for. No other manual corrections are to be made for the purposes of the present invention.

By a polypeptide having an amino acid sequence at least, for example, 95% "identical" to a query amino acid sequence of the present invention, it is intended that the amino acid sequence of the subject polypeptide is identical to the query sequence except that the subject polypeptide sequence may include up to five amino acid alterations per each 100 amino acids of the query amino acid sequence. In other words, to obtain a polypeptide having an amino acid sequence at least 95% identical to a query

amino acid sequence, up to 5% of the amino acid residues in the subject sequence may be inserted, deleted, (indels) or substituted with another amino acid. These alterations of the reference sequence may occur at the amino or carboxy terminal positions of the reference amino acid sequence or anywhere between those terminal positions,  
5 interspersed either individually among residues in the reference sequence or in one or more contiguous groups within the reference sequence.

As a practical matter, whether any particular polypeptide is at least 90%, 95%, 96%, 97%, 98% or 99% identical to, for instance, the amino acid sequences shown in Table 1 or to the amino acid sequence encoded by deposited DNA clone can be  
10 determined conventionally using known computer programs. A preferred method for determining the best overall match between a query sequence (a sequence of the present invention) and a subject sequence, also referred to as a global sequence alignment, can be determined using the FASTDB computer program based on the algorithm of Brutlag et al. (Comp. App. Biosci. (1990) 6:237-245). In a sequence alignment the query and  
15 subject sequences are either both nucleotide sequences or both amino acid sequences. The result of said global sequence alignment is in percent identity. Preferred parameters used in a FASTDB amino acid alignment are: Matrix=PAM 0, k-tuple=2, Mismatch Penalty=1, Joining Penalty=20, Randomization Group Length=0, Cutoff Score=1, Window Size=sequence length, Gap Penalty=5, Gap Size Penalty=0.05, Window  
20 Size=500 or the length of the subject amino acid sequence, whichever is shorter.

If the subject sequence is shorter than the query sequence due to N- or C-terminal deletions, not because of internal deletions, a manual correction must be made to the results. This is because the FASTDB program does not account for N- and C-terminal truncations of the subject sequence when calculating global percent identity.  
25 For subject sequences truncated at the N- and C-termini, relative to the the query sequence, the percent identity is corrected by calculating the number of residues of the query sequence that are N- and C-terminal of the subject sequence, which are not matched/aligned with a corresponding subject residue, as a percent of the total bases of the query sequence. Whether a residue is matched/aligned is determined by results of  
30 the FASTDB sequence alignment. This percentage is then subtracted from the percent identity, calculated by the above FASTDB program using the specified parameters, to arrive at a final percent identity score. This final percent identity score is what is used for the purposes of the present invention. Only residues to the N- and C-termini of the subject sequence, which are not matched/aligned with the query sequence, are  
35 considered for the purposes of manually adjusting the percent identity score. That is, only query residue positions outside the farthest N- and C-terminal residues of the subject sequence.

For example, a 90 amino acid residue subject sequence is aligned with a 100 residue query sequence to determine percent identity. The deletion occurs at the N-terminus of the subject sequence and therefore, the FASTDB alignment does not show a matching/alignment of the first 10 residues at the N-terminus. The 10 unpaired  
5 residues represent 10% of the sequence (number of residues at the N- and C- termini not matched/total number of residues in the query sequence) so 10% is subtracted from the percent identity score calculated by the FASTDB program. If the remaining 90 residues were perfectly matched the final percent identity would be 90%. In another example, a 90 residue subject sequence is compared with a 100 residue query sequence.  
10 This time the deletions are internal deletions so there are no residues at the N- or C-termini of the subject sequence which are not matched/aligned with the query. In this case the percent identity calculated by FASTDB is not manually corrected. Once again, only residue positions outside the N- and C-terminal ends of the subject sequence, as displayed in the FASTDB alignment, which are not matched/aligned with the query  
15 sequence are manually corrected for. No other manual corrections are to be made for the purposes of the present invention.

The variants may contain alterations in the coding regions, non-coding regions, or both. Especially preferred are polynucleotide variants containing alterations which produce silent substitutions, additions, or deletions, but do not alter the properties or  
20 activities of the encoded polypeptide. Nucleotide variants produced by silent substitutions due to the degeneracy of the genetic code are preferred. Moreover, variants in which 5-10, 1-5, or 1-2 amino acids are substituted, deleted, or added in any combination are also preferred. Polynucleotide variants can be produced for a variety of reasons, e.g., to optimize codon expression for a particular host (change codons in  
25 the human mRNA to those preferred by a bacterial host such as *E. coli*).

Naturally occurring variants are called "allelic variants," and refer to one of several alternate forms of a gene occupying a given locus on a chromosome of an organism. (Genes II, Lewin, B., ed., John Wiley & Sons, New York (1985).) These allelic variants can vary at either the polynucleotide and/or polypeptide level.  
30 Alternatively, non-naturally occurring variants may be produced by mutagenesis techniques or by direct synthesis.

Using known methods of protein engineering and recombinant DNA technology, variants may be generated to improve or alter the characteristics of the polypeptides of the present invention. For instance, one or more amino acids can be  
35 deleted from the N-terminus or C-terminus of the secreted protein without substantial loss of biological function. The authors of Ron et al., *J. Biol. Chem.* 268: 2984-2988 (1993), reported variant KGF proteins having heparin binding activity even after

deleting 3, 8, or 27 amino-terminal amino acid residues. Similarly, Interferon gamma exhibited up to ten times higher activity after deleting 8-10 amino acid residues from the carboxy terminus of this protein. (Dobeli et al., J. Biotechnology 7:199-216 (1988).)

Moreover, ample evidence demonstrates that variants often retain a biological activity similar to that of the naturally occurring protein. For example, Gayle and coworkers (J. Biol. Chem 268:22105-22111 (1993)) conducted extensive mutational analysis of human cytokine IL-1a. They used random mutagenesis to generate over 3,500 individual IL-1a mutants that averaged 2.5 amino acid changes per variant over the entire length of the molecule. Multiple mutations were examined at every possible amino acid position. The investigators found that "[m]ost of the molecule could be altered with little effect on either [binding or biological activity]." (See, Abstract.) In fact, only 23 unique amino acid sequences, out of more than 3,500 nucleotide sequences examined, produced a protein that significantly differed in activity from wild-type.

Furthermore, even if deleting one or more amino acids from the N-terminus or C-terminus of a polypeptide results in modification or loss of one or more biological functions, other biological activities may still be retained. For example, the ability of a deletion variant to induce and/or to bind antibodies which recognize the secreted form will likely be retained when less than the majority of the residues of the secreted form are removed from the N-terminus or C-terminus. Whether a particular polypeptide lacking N- or C-terminal residues of a protein retains such immunogenic activities can readily be determined by routine methods described herein and otherwise known in the art.

Thus, the invention further includes polypeptide variants which show substantial biological activity. Such variants include deletions, insertions, inversions, repeats, and substitutions selected according to general rules known in the art so as have little effect on activity. For example, guidance concerning how to make phenotypically silent amino acid substitutions is provided in Bowie, J. U. et al., Science 247:1306-1310 (1990), wherein the authors indicate that there are two main strategies for studying the tolerance of an amino acid sequence to change.

The first strategy exploits the tolerance of amino acid substitutions by natural selection during the process of evolution. By comparing amino acid sequences in different species, conserved amino acids can be identified. These conserved amino acids are likely important for protein function. In contrast, the amino acid positions where substitutions have been tolerated by natural selection indicates that these positions are not critical for protein function. Thus, positions tolerating amino acid substitution could be modified while still maintaining biological activity of the protein.

The second strategy uses genetic engineering to introduce amino acid changes at specific positions of a cloned gene to identify regions critical for protein function. For example, site directed mutagenesis or alanine-scanning mutagenesis (introduction of single alanine mutations at every residue in the molecule) can be used. (Cunningham and Wells, Science 244:1081-1085 (1989).) The resulting mutant molecules can then be tested for biological activity.

As the authors state, these two strategies have revealed that proteins are surprisingly tolerant of amino acid substitutions. The authors further indicate which amino acid changes are likely to be permissive at certain amino acid positions in the protein. For example, most buried (within the tertiary structure of the protein) amino acid residues require nonpolar side chains, whereas few features of surface side chains are generally conserved. Moreover, tolerated conservative amino acid substitutions involve replacement of the aliphatic or hydrophobic amino acids Ala, Val, Leu and Ile; replacement of the hydroxyl residues Ser and Thr; replacement of the acidic residues Asp and Glu; replacement of the amide residues Asn and Gln, replacement of the basic residues Lys, Arg, and His; replacement of the aromatic residues Phe, Tyr, and Trp, and replacement of the small-sized amino acids Ala, Ser, Thr, Met, and Gly.

Besides conservative amino acid substitution, variants of the present invention include (i) substitutions with one or more of the non-conserved amino acid residues, where the substituted amino acid residues may or may not be one encoded by the genetic code, or (ii) substitution with one or more of amino acid residues having a substituent group, or (iii) fusion of the mature polypeptide with another compound, such as a compound to increase the stability and/or solubility of the polypeptide (for example, polyethylene glycol), or (iv) fusion of the polypeptide with additional amino acids, such as an IgG Fc fusion region peptide, or leader or secretory sequence, or a sequence facilitating purification. Such variant polypeptides are deemed to be within the scope of those skilled in the art from the teachings herein.

For example, polypeptide variants containing amino acid substitutions of charged amino acids with other charged or neutral amino acids may produce proteins with improved characteristics, such as less aggregation. Aggregation of pharmaceutical formulations both reduces activity and increases clearance due to the aggregate's immunogenic activity. (Pinckard et al., Clin. Exp. Immunol. 2:331-340 (1967); Robbins et al., Diabetes 36: 838-845 (1987); Cleland et al., Crit. Rev. Therapeutic Drug Carrier Systems 10:307-377 (1993).)

### **Polynucleotide and Polypeptide Fragments**

In the present invention, a "polynucleotide fragment" refers to a short polynucleotide having a nucleic acid sequence contained in the deposited clone or shown in SEQ ID NO:X. The short nucleotide fragments are preferably at least about 15 nt, and more preferably at least about 20 nt, still more preferably at least about 30 nt, and even more preferably, at least about 40 nt in length. A fragment "at least 20 nt in length," for example, is intended to include 20 or more contiguous bases from the cDNA sequence contained in the deposited clone or the nucleotide sequence shown in SEQ ID NO:X. These nucleotide fragments are useful as diagnostic probes and primers as discussed herein. Of course, larger fragments (e.g., 50, 150, 500, 600, 2000 nucleotides) are preferred.

Moreover, representative examples of polynucleotide fragments of the invention, include, for example, fragments having a sequence from about nucleotide number 1-50, 51-100, 101-150, 151-200, 201-250, 251-300, 301-350, 351-400, 401-450, 451-500, 501-550, 551-600, 651-700, 701-750, 751-800, 800-850, 851-900, 901-950, 951-1000, 1001-1050, 1051-1100, 1101-1150, 1151-1200, 1201-1250, 1251-1300, 1301-1350, 1351-1400, 1401-1450, 1451-1500, 1501-1550, 1551-1600, 1601-1650, 1651-1700, 1701-1750, 1751-1800, 1801-1850, 1851-1900, 1901-1950, 1951-2000, or 2001 to the end of SEQ ID NO:X or the cDNA contained in the deposited clone. In this context "about" includes the particularly recited ranges, larger or smaller by several (5, 4, 3, 2, or 1) nucleotides, at either terminus or at both termini. Preferably, these fragments encode a polypeptide which has biological activity. More preferably, these polynucleotides can be used as probes or primers as discussed herein.

In the present invention, a "polypeptide fragment" refers to a short amino acid sequence contained in SEQ ID NO:Y or encoded by the cDNA contained in the deposited clone. Protein fragments may be "free-standing," or comprised within a larger polypeptide of which the fragment forms a part or region, most preferably as a single continuous region. Representative examples of polypeptide fragments of the invention, include, for example, fragments from about amino acid number 1-20, 21-40, 41-60, 61-80, 81-100, 102-120, 121-140, 141-160, or 161 to the end of the coding region. Moreover, polypeptide fragments can be about 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, 120, 130, 140, or 150 amino acids in length. In this context "about" includes the particularly recited ranges, larger or smaller by several (5, 4, 3, 2, or 1) amino acids, at either extreme or at both extremes.

Preferred polypeptide fragments include the secreted protein as well as the mature form. Further preferred polypeptide fragments include the secreted protein or the mature form having a continuous series of deleted residues from the amino or the carboxy terminus, or both. For example, any number of amino acids, ranging from 1-



60, can be deleted from the amino terminus of either the secreted polypeptide or the mature form. Similarly, any number of amino acids, ranging from 1-30, can be deleted from the carboxy terminus of the secreted protein or mature form. Furthermore, any combination of the above amino and carboxy terminus deletions are preferred.

- 5 Similarly, polynucleotide fragments encoding these polypeptide fragments are also preferred.

Particularly, N-terminal deletions of the polypeptide of the present invention can be described by the general formula m-p, where p is the total number of amino acids in the polypeptide and m is an integer from 2 to (p-1), and where both of these integers (m  
10 & p) correspond to the position of the amino acid residue identified in SEQ ID NO:Y.

Moreover, C-terminal deletions of the polypeptide of the present invention can also be described by the general formula 1-n, where n is an integer from 2 to (p-1), and again where these integers (n & p) correspond to the position of the amino acid residue identified in SEQ ID NO:Y.

- 15 The invention also provides polypeptides having one or more amino acids deleted from both the amino and the carboxyl termini, which may be described generally as having residues m-n of SEQ ID NO:Y, where m and n are integers as described above.

Also preferred are polypeptide and polynucleotide fragments characterized by  
20 structural or functional domains, such as fragments that comprise alpha-helix and alpha-helix forming regions, beta-sheet and beta-sheet-forming regions, turn and turn-forming regions, coil and coil-forming regions, hydrophilic regions, hydrophobic regions, alpha amphipathic regions, beta amphipathic regions, flexible regions, surface-forming regions, substrate binding region, and high antigenic index regions.

- 25 Polypeptide fragments of SEQ ID NO:Y falling within conserved domains are specifically contemplated by the present invention. Moreover, polynucleotide fragments encoding these domains are also contemplated.

Other preferred fragments are biologically active fragments. Biologically active fragments are those exhibiting activity similar, but not necessarily identical, to an  
30 activity of the polypeptide of the present invention. The biological activity of the fragments may include an improved desired activity, or a decreased undesirable activity.

### **Epitopes & Antibodies**

- 35 In the present invention, "epitopes" refer to polypeptide fragments having antigenic or immunogenic activity in an animal, especially in a human. A preferred embodiment of the present invention relates to a polypeptide fragment comprising an epitope, as well as the polynucleotide encoding this fragment. A region of a protein

molecule to which an antibody can bind is defined as an "antigenic epitope." In contrast, an "immunogenic epitope" is defined as a part of a protein that elicits an antibody response. (See, for instance, Geysen et al., Proc. Natl. Acad. Sci. USA 81:3998- 4002 (1983).)

- 5           Fragments which function as epitopes may be produced by any conventional means. (See, e.g., Houghten, R. A., Proc. Natl. Acad. Sci. USA 82:5131-5135 (1985) further described in U.S. Patent No. 4,631,211.)

          In the present invention, antigenic epitopes preferably contain a sequence of at least seven, more preferably at least nine, and most preferably between about 15 to  
10   about 30 amino acids. Antigenic epitopes are useful to raise antibodies, including monoclonal antibodies, that specifically bind the epitope. (See, for instance, Wilson et al., Cell 37:767-778 (1984); Sutcliffe, J. G. et al., Science 219:660-666 (1983).)

- Similarly, immunogenic epitopes can be used to induce antibodies according to methods well known in the art. (See, for instance, Sutcliffe et al., supra; Wilson et al.,  
15   supra; Chow, M. et al., Proc. Natl. Acad. Sci. USA 82:910-914; and Bittle, F. J. et al., J. Gen. Virol. 66:2347-2354 (1985).) A preferred immunogenic epitope includes the secreted protein. The immunogenic epitopes may be presented together with a carrier protein, such as an albumin, to an animal system (such as rabbit or mouse) or, if it is long enough (at least about 25 amino acids), without a carrier. However,  
20   immunogenic epitopes comprising as few as 8 to 10 amino acids have been shown to be sufficient to raise antibodies capable of binding to, at the very least, linear epitopes in a denatured polypeptide (e.g., in Western blotting.)

- As used herein, the term "antibody" (Ab) or "monoclonal antibody" (Mab) is meant to include intact molecules as well as antibody fragments (such as, for example,  
25   Fab and F(ab')<sub>2</sub> fragments) which are capable of specifically binding to protein. Fab and F(ab')<sub>2</sub> fragments lack the Fc fragment of intact antibody, clear more rapidly from the circulation, and may have less non-specific tissue binding than an intact antibody. (Wahl et al., J. Nucl. Med. 24:316-325 (1983).) Thus, these fragments are preferred, as well as the products of a FAB or other immunoglobulin expression library.

- 30   Moreover, antibodies of the present invention include chimeric, single chain, and humanized antibodies.

### **Fusion Proteins**

- Any polypeptide of the present invention can be used to generate fusion  
35   proteins. For example, the polypeptide of the present invention, when fused to a second protein, can be used as an antigenic tag. Antibodies raised against the polypeptide of the present invention can be used to indirectly detect the second protein

by binding to the polypeptide. Moreover, because secreted proteins target cellular locations based on trafficking signals, the polypeptides of the present invention can be used as targeting molecules once fused to other proteins.

5 Examples of domains that can be fused to polypeptides of the present invention include not only heterologous signal sequences, but also other heterologous functional regions. The fusion does not necessarily need to be direct, but may occur through linker sequences.

Moreover, fusion proteins may also be engineered to improve characteristics of the polypeptide of the present invention. For instance, a region of additional amino  
10 acids, particularly charged amino acids, may be added to the N-terminus of the polypeptide to improve stability and persistence during purification from the host cell or subsequent handling and storage. Also, peptide moieties may be added to the polypeptide to facilitate purification. Such regions may be removed prior to final preparation of the polypeptide. The addition of peptide moieties to facilitate handling of  
15 polypeptides are familiar and routine techniques in the art.

Moreover, polypeptides of the present invention, including fragments, and specifically epitopes, can be combined with parts of the constant domain of immunoglobulins (IgG), resulting in chimeric polypeptides. These fusion proteins facilitate purification and show an increased half-life in vivo. One reported example  
20 describes chimeric proteins consisting of the first two domains of the human CD4-polypeptide and various domains of the constant regions of the heavy or light chains of mammalian immunoglobulins. (EP A 394,827; Traunecker et al., Nature 331:84-86 (1988).) Fusion proteins having disulfide-linked dimeric structures (due to the IgG) can also be more efficient in binding and neutralizing other molecules, than the  
25 monomeric secreted protein or protein fragment alone. (Fountoulakis et al., J. Biochem. 270:3958-3964 (1995).)

Similarly, EP-A-O 464 533 (Canadian counterpart 2045869) discloses fusion proteins comprising various portions of constant region of immunoglobulin molecules together with another human protein or part thereof. In many cases, the Fc part in a  
30 fusion protein is beneficial in therapy and diagnosis, and thus can result in, for example, improved pharmacokinetic properties. (EP-A 0232 262.) Alternatively, deleting the Fc part after the fusion protein has been expressed, detected, and purified, would be desired. For example, the Fc portion may hinder therapy and diagnosis if the fusion protein is used as an antigen for immunizations. In drug discovery, for  
35 example, human proteins, such as hIL-5, have been fused with Fc portions for the purpose of high-throughput screening assays to identify antagonists of hIL-5. (See, D.

Bennett et al., J. Molecular Recognition 8:52-58 (1995); K. Johanson et al., J. Biol. Chem. 270:9459-9471 (1995).)

Moreover, the polypeptides of the present invention can be fused to marker sequences, such as a peptide which facilitates purification of the fused polypeptide. In preferred embodiments, the marker amino acid sequence is a hexa-histidine peptide, such as the tag provided in a pQE vector (QIAGEN, Inc., 9259 Eton Avenue, Chatsworth, CA, 91311), among others, many of which are commercially available. As described in Gentz et al., Proc. Natl. Acad. Sci. USA 86:821-824 (1989), for instance, hexa-histidine provides for convenient purification of the fusion protein. Another peptide tag useful for purification, the "HA" tag, corresponds to an epitope derived from the influenza hemagglutinin protein. (Wilson et al., Cell 37:767 (1984).)

Thus, any of these above fusions can be engineered using the polynucleotides or the polypeptides of the present invention.

#### 15 Vectors, Host Cells, and Protein Production

The present invention also relates to vectors containing the polynucleotide of the present invention, host cells, and the production of polypeptides by recombinant techniques. The vector may be, for example, a phage, plasmid, viral, or retroviral vector. Retroviral vectors may be replication competent or replication defective. In the latter case, viral propagation generally will occur only in complementing host cells.

The polynucleotides may be joined to a vector containing a selectable marker for propagation in a host. Generally, a plasmid vector is introduced in a precipitate, such as a calcium phosphate precipitate, or in a complex with a charged lipid. If the vector is a virus, it may be packaged in vitro using an appropriate packaging cell line and then transduced into host cells.

The polynucleotide insert should be operatively linked to an appropriate promoter, such as the phage lambda PL promoter, the E. coli lac, trp, phoA and tac promoters, the SV40 early and late promoters and promoters of retroviral LTRs, to name a few. Other suitable promoters will be known to the skilled artisan. The expression constructs will further contain sites for transcription initiation, termination, and, in the transcribed region, a ribosome binding site for translation. The coding portion of the transcripts expressed by the constructs will preferably include a translation initiating codon at the beginning and a termination codon (UAA, UGA or UAG) appropriately positioned at the end of the polypeptide to be translated.

As indicated, the expression vectors will preferably include at least one selectable marker. Such markers include dihydrofolate reductase, G418 or neomycin resistance for eukaryotic cell culture and tetracycline, kanamycin or ampicillin resistance

genes for culturing in *E. coli* and other bacteria. Representative examples of appropriate hosts include, but are not limited to, bacterial cells, such as *E. coli*, *Streptomyces* and *Salmonella typhimurium* cells; fungal cells, such as yeast cells; insect cells such as *Drosophila* S2 and *Spodoptera* Sf9 cells; animal cells such as CHO, COS, 293, and Bowes melanoma cells; and plant cells. Appropriate culture mediums and conditions for the above-described host cells are known in the art.

Among vectors preferred for use in bacteria include pQE70, pQE60 and pQE-9, available from QIAGEN, Inc.; pBluescript vectors, Phagescript vectors, pNH8A, pNH16a, pNH18A, pNH46A, available from Stratagene Cloning Systems, Inc.; and p

Introduction of the construct into the host cell can be effected by calcium phosphate transfection, DEAE-dextran mediated transfection, cationic lipid-mediated transfection, electroporation, transduction, infection, or other methods. Such methods are described in many standard laboratory manuals, such as Davis et al., *Basic Methods In Molecular Biology* (1986). It is specifically contemplated that the polypeptides of the present invention may in fact be expressed by a host cell lacking a recombinant vector.

A polypeptide of this invention can be recovered and purified from recombinant cell cultures by well-known methods including ammonium sulfate or ethanol precipitation, acid extraction, anion or cation exchange chromatography, phosphocellulose chromatography, hydrophobic interaction chromatography, affinity chromatography, hydroxylapatite chromatography and lectin chromatography. Most preferably, high performance liquid chromatography ("HPLC") is employed for purification.

Polypeptides of the present invention, and preferably the secreted form, can also be recovered from: products purified from natural sources, including bodily fluids, tissues and cells, whether directly isolated or cultured; products of chemical synthetic procedures; and products produced by recombinant techniques from a prokaryotic or eukaryotic host, including, for example, bacterial, yeast, higher plant, insect, and mammalian cells. Depending upon the host employed in a recombinant production procedure, the polypeptides of the present invention may be glycosylated or may be non-glycosylated. In addition, polypeptides of the invention may also include an initial modified methionine residue, in some cases as a result of host-mediated processes. Thus, it is well known in the art that the N-terminal methionine encoded by the translation initiation codon generally is removed with high efficiency from any protein

after translation in all eukaryotic cells. While the N-terminal methionine on most proteins also is efficiently removed in most prokaryotes, for some proteins, this prokaryotic removal process is inefficient, depending on the nature of the amino acid to which the N-terminal methionine is covalently linked.

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### Uses of the Polynucleotides

Each of the polynucleotides identified herein can be used in numerous ways as reagents. The following description should be considered exemplary and utilizes known techniques.

10 The polynucleotides of the present invention are useful for chromosome identification. There exists an ongoing need to identify new chromosome markers, since few chromosome marking reagents, based on actual sequence data (repeat polymorphisms), are presently available. Each polynucleotide of the present invention can be used as a chromosome marker.

15 Briefly, sequences can be mapped to chromosomes by preparing PCR primers (preferably 15-25 bp) from the sequences shown in SEQ ID NO:X. Primers can be selected using computer analysis so that primers do not span more than one predicted exon in the genomic DNA. These primers are then used for PCR screening of somatic cell hybrids containing individual human chromosomes. Only those hybrids containing  
20 the human gene corresponding to the SEQ ID NO:X will yield an amplified fragment.

Similarly, somatic hybrids provide a rapid method of PCR mapping the polynucleotides to particular chromosomes. Three or more clones can be assigned per day using a single thermal cycler. Moreover, sublocalization of the polynucleotides can be achieved with panels of specific chromosome fragments. Other gene mapping  
25 strategies that can be used include in situ hybridization, prescreening with labeled flow-sorted chromosomes, and preselection by hybridization to construct chromosome specific-cDNA libraries.

Precise chromosomal location of the polynucleotides can also be achieved using fluorescence in situ hybridization (FISH) of a metaphase chromosomal spread. This  
30 technique uses polynucleotides as short as 500 or 600 bases; however, polynucleotides 2,000-4,000 bp are preferred. For a review of this technique, see Verma et al., "Human Chromosomes: a Manual of Basic Techniques," Pergamon Press, New York (1988).

For chromosome mapping, the polynucleotides can be used individually (to  
35 mark a single chromosome or a single site on that chromosome) or in panels (for marking multiple sites and/or multiple chromosomes). Preferred polynucleotides correspond to the noncoding regions of the cDNAs because the coding sequences are

more likely conserved within gene families, thus increasing the chance of cross hybridization during chromosomal mapping.

Once a polynucleotide has been mapped to a precise chromosomal location, the physical position of the polynucleotide can be used in linkage analysis. Linkage analysis establishes coinheritance between a chromosomal location and presentation of a particular disease. (Disease mapping data are found, for example, in V. McKusick, Mendelian Inheritance in Man (available on line through Johns Hopkins University Welch Medical Library) .) Assuming 1 megabase mapping resolution and one gene per 20 kb, a cDNA precisely localized to a chromosomal region associated with the disease could be one of 50-500 potential causative genes.

Thus, once coinheritance is established, differences in the polynucleotide and the corresponding gene between affected and unaffected individuals can be examined. First, visible structural alterations in the chromosomes, such as deletions or translocations, are examined in chromosome spreads or by PCR. If no structural alterations exist, the presence of point mutations are ascertained. Mutations observed in some or all affected individuals, but not in normal individuals, indicates that the mutation may cause the disease. However, complete sequencing of the polypeptide and the corresponding gene from several normal individuals is required to distinguish the mutation from a polymorphism. If a new polymorphism is identified, this polymorphic polypeptide can be used for further linkage analysis.

Furthermore, increased or decreased expression of the gene in affected individuals as compared to unaffected individuals can be assessed using polynucleotides of the present invention. Any of these alterations (altered expression, chromosomal rearrangement, or mutation) can be used as a diagnostic or prognostic marker.

In addition to the foregoing, a polynucleotide can be used to control gene expression through triple helix formation or antisense DNA or RNA. Both methods rely on binding of the polynucleotide to DNA or RNA. For these techniques, preferred polynucleotides are usually 20 to 40 bases in length and complementary to either the region of the gene involved in transcription (triple helix - see Lee et al., Nucl. Acids Res. 6:3073 (1979); Cooney et al., Science 241:456 (1988); and Dervan et al., Science 251:1360 (1991) ) or to the mRNA itself (antisense - Okano, J. Neurochem. 56:560 (1991); Oligodeoxy-nucleotides as Antisense Inhibitors of Gene Expression, CRC Press, Boca Raton, FL (1988).) Triple helix formation optimally results in a shut-off of RNA transcription from DNA, while antisense RNA hybridization blocks translation of an mRNA molecule into polypeptide. Both techniques are effective in model

systems, and the information disclosed herein can be used to design antisense or triple helix polynucleotides in an effort to treat disease.

Polynucleotides of the present invention are also useful in gene therapy. One goal of gene therapy is to insert a normal gene into an organism having a defective gene, in an effort to correct the genetic defect. The polynucleotides disclosed in the present invention offer a means of targeting such genetic defects in a highly accurate manner. Another goal is to insert a new gene that was not present in the host genome, thereby producing a new trait in the host cell.

The polynucleotides are also useful for identifying individuals from minute biological samples. The United States military, for example, is considering the use of restriction fragment length polymorphism (RFLP) for identification of its personnel. In this technique, an individual's genomic DNA is digested with one or more restriction enzymes, and probed on a Southern blot to yield unique bands for identifying personnel. This method does not suffer from the current limitations of "Dog Tags" which can be lost, switched, or stolen, making positive identification difficult. The polynucleotides of the present invention can be used as additional DNA markers for RFLP.

The polynucleotides of the present invention can also be used as an alternative to RFLP, by determining the actual base-by-base DNA sequence of selected portions of an individual's genome. These sequences can be used to prepare PCR primers for amplifying and isolating such selected DNA, which can then be sequenced. Using this technique, individuals can be identified because each individual will have a unique set of DNA sequences. Once an unique ID database is established for an individual, positive identification of that individual, living or dead, can be made from extremely small tissue samples.

Forensic biology also benefits from using DNA-based identification techniques as disclosed herein. DNA sequences taken from very small biological samples such as tissues, e.g., hair or skin, or body fluids, e.g., blood, saliva, semen, etc., can be amplified using PCR. In one prior art technique, gene sequences amplified from polymorphic loci, such as DQa class II HLA gene, are used in forensic biology to identify individuals. (Erlich, H., PCR Technology, Freeman and Co. (1992).) Once these specific polymorphic loci are amplified, they are digested with one or more restriction enzymes, yielding an identifying set of bands on a Southern blot probed with DNA corresponding to the DQa class II HLA gene. Similarly, polynucleotides of the present invention can be used as polymorphic markers for forensic purposes.

There is also a need for reagents capable of identifying the source of a particular tissue. Such need arises, for example, in forensics when presented with tissue of



unknown origin. Appropriate reagents can comprise, for example, DNA probes or primers specific to particular tissue prepared from the sequences of the present invention. Panels of such reagents can identify tissue by species and/or by organ type. In a similar fashion, these reagents can be used to screen tissue cultures for  
5 contamination.

In the very least, the polynucleotides of the present invention can be used as molecular weight markers on Southern gels, as diagnostic probes for the presence of a specific mRNA in a particular cell type, as a probe to "subtract-out" known sequences in the process of discovering novel polynucleotides, for selecting and making oligomers  
10 for attachment to a "gene chip" or other support, to raise anti-DNA antibodies using DNA immunization techniques, and as an antigen to elicit an immune response.

#### Uses of the Polypeptides

Each of the polypeptides identified herein can be used in numerous ways. The  
15 following description should be considered exemplary and utilizes known techniques.

A polypeptide of the present invention can be used to assay protein levels in a biological sample using antibody-based techniques. For example, protein expression in tissues can be studied with classical immunohistological methods. (Jalkanen, M., et al., J. Cell. Biol. 101:976-985 (1985); Jalkanen, M., et al., J. Cell . Biol. 105:3087-  
20 3096 (1987).) Other antibody-based methods useful for detecting protein gene expression include immunoassays, such as the enzyme linked immunosorbent assay (ELISA) and the radioimmunoassay (RIA). Suitable antibody assay labels are known in the art and include enzyme labels, such as, glucose oxidase, and radioisotopes, such as iodine (125I, 121I), carbon (14C), sulfur (35S), tritium (3H), indium (112In), and  
25 technetium (99mTc), and fluorescent labels, such as fluorescein and rhodamine, and biotin.

In addition to assaying secreted protein levels in a biological sample, proteins can also be detected in vivo by imaging. Antibody labels or markers for in vivo imaging of protein include those detectable by X-radiography, NMR or ESR. For X-  
30 radiography, suitable labels include radioisotopes such as barium or cesium, which emit detectable radiation but are not overtly harmful to the subject. Suitable markers for NMR and ESR include those with a detectable characteristic spin, such as deuterium, which may be incorporated into the antibody by labeling of nutrients for the relevant hybridoma.

35 A protein-specific antibody or antibody fragment which has been labeled with an appropriate detectable imaging moiety, such as a radioisotope (for example, 131I, 112In, 99mTc), a radio-opaque substance, or a material detectable by nuclear magnetic

resonance, is introduced (for example, parenterally, subcutaneously, or intraperitoneally) into the mammal. It will be understood in the art that the size of the subject and the imaging system used will determine the quantity of imaging moiety needed to produce diagnostic images. In the case of a radioisotope moiety, for a human  
5 subject, the quantity of radioactivity injected will normally range from about 5 to 20 millicuries of <sup>99m</sup>Tc. The labeled antibody or antibody fragment will then preferentially accumulate at the location of cells which contain the specific protein. In vivo tumor imaging is described in S.W. Burchiel et al., "Immunopharmacokinetics of Radiolabeled Antibodies and Their Fragments." (Chapter 13 in Tumor Imaging: The  
10 Radiochemical Detection of Cancer, S.W. Burchiel and B. A. Rhodes, eds., Masson Publishing Inc. (1982).)

Thus, the invention provides a diagnostic method of a disorder, which involves (a) assaying the expression of a polypeptide of the present invention in cells or body fluid of an individual; (b) comparing the level of gene expression with a standard gene  
15 expression level, whereby an increase or decrease in the assayed polypeptide gene expression level compared to the standard expression level is indicative of a disorder.

Moreover, polypeptides of the present invention can be used to treat disease. For example, patients can be administered a polypeptide of the present invention in an effort to replace absent or decreased levels of the polypeptide (e.g., insulin), to  
20 supplement absent or decreased levels of a different polypeptide (e.g., hemoglobin S for hemoglobin B), to inhibit the activity of a polypeptide (e.g., an oncogene), to activate the activity of a polypeptide (e.g., by binding to a receptor), to reduce the activity of a membrane bound receptor by competing with it for free ligand (e.g., soluble TNF receptors used in reducing inflammation), or to bring about a desired  
25 response (e.g., blood vessel growth).

Similarly, antibodies directed to a polypeptide of the present invention can also be used to treat disease. For example, administration of an antibody directed to a polypeptide of the present invention can bind and reduce overproduction of the polypeptide. Similarly, administration of an antibody can activate the polypeptide, such  
30 as by binding to a polypeptide bound to a membrane (receptor).

At the very least, the polypeptides of the present invention can be used as molecular weight markers on SDS-PAGE gels or on molecular sieve gel filtration columns using methods well known to those of skill in the art. Polypeptides can also be used to raise antibodies, which in turn are used to measure protein expression from a  
35 recombinant cell, as a way of assessing transformation of the host cell. Moreover, the polypeptides of the present invention can be used to test the following biological activities.

### **Biological Activities**

The polynucleotides and polypeptides of the present invention can be used in assays to test for one or more biological activities. If these polynucleotides and polypeptides do exhibit activity in a particular assay, it is likely that these molecules may be involved in the diseases associated with the biological activity. Thus, the polynucleotides and polypeptides could be used to treat the associated disease.

### **Immune Activity**

A polypeptide or polynucleotide of the present invention may be useful in treating deficiencies or disorders of the immune system, by activating or inhibiting the proliferation, differentiation, or mobilization (chemotaxis) of immune cells. Immune cells develop through a process called hematopoiesis, producing myeloid (platelets, red blood cells, neutrophils, and macrophages) and lymphoid (B and T lymphocytes) cells from pluripotent stem cells. The etiology of these immune deficiencies or disorders may be genetic, somatic, such as cancer or some autoimmune disorders, acquired (e.g., by chemotherapy or toxins), or infectious. Moreover, a polynucleotide or polypeptide of the present invention can be used as a marker or detector of a particular immune system disease or disorder.

A polynucleotide or polypeptide of the present invention may be useful in treating or detecting deficiencies or disorders of hematopoietic cells. A polypeptide or polynucleotide of the present invention could be used to increase differentiation and proliferation of hematopoietic cells, including the pluripotent stem cells, in an effort to treat those disorders associated with a decrease in certain (or many) types hematopoietic cells. Examples of immunologic deficiency syndromes include, but are not limited to: blood protein disorders (e.g. agammaglobulinemia, dysgammaglobulinemia), ataxia telangiectasia, common variable immunodeficiency, Digeorge Syndrome, HIV infection, HTLV-BLV infection, leukocyte adhesion deficiency syndrome, lymphopenia, phagocyte bactericidal dysfunction, severe combined immunodeficiency (SCIDs), Wiskott-Aldrich Disorder, anemia, thrombocytopenia, or hemoglobinuria.

Moreover, a polypeptide or polynucleotide of the present invention could also be used to modulate hemostatic (the stopping of bleeding) or thrombolytic activity (clot formation). For example, by increasing hemostatic or thrombolytic activity, a polynucleotide or polypeptide of the present invention could be used to treat blood coagulation disorders (e.g., afibrinogenemia, factor deficiencies), blood platelet disorders (e.g. thrombocytopenia), or wounds resulting from trauma, surgery, or other causes. Alternatively, a polynucleotide or polypeptide of the present invention that can

decrease hemostatic or thrombolytic activity could be used to inhibit or dissolve clotting. These molecules could be important in the treatment of heart attacks (infarction), strokes, or scarring.

5 A polynucleotide or polypeptide of the present invention may also be useful in treating or detecting autoimmune disorders. Many autoimmune disorders result from inappropriate recognition of self as foreign material by immune cells. This inappropriate recognition results in an immune response leading to the destruction of the host tissue. Therefore, the administration of a polypeptide or polynucleotide of the present invention that inhibits an immune response, particularly the proliferation,  
10 differentiation, or chemotaxis of T-cells, may be an effective therapy in preventing autoimmune disorders.

Examples of autoimmune disorders that can be treated or detected by the present invention include, but are not limited to: Addison's Disease, hemolytic anemia, antiphospholipid syndrome, rheumatoid arthritis, dermatitis, allergic encephalomyelitis,  
15 glomerulonephritis, Goodpasture's Syndrome, Graves' Disease, Multiple Sclerosis, Myasthenia Gravis, Neuritis, Ophthalmia, Bullous Pemphigoid, Pemphigus, Polyendocrinopathies, Purpura, Reiter's Disease, Stiff-Man Syndrome, Autoimmune Thyroiditis, Systemic Lupus Erythematosus, Autoimmune Pulmonary Inflammation, Guillain-Barre Syndrome, insulin dependent diabetes mellitus, and autoimmune  
20 inflammatory eye disease.

Similarly, allergic reactions and conditions, such as asthma (particularly allergic asthma) or other respiratory problems, may also be treated by a polypeptide or polynucleotide of the present invention. Moreover, these molecules can be used to treat anaphylaxis, hypersensitivity to an antigenic molecule, or blood group incompatibility.

25 A polynucleotide or polypeptide of the present invention may also be used to treat and/or prevent organ rejection or graft-versus-host disease (GVHD). Organ rejection occurs by host immune cell destruction of the transplanted tissue through an immune response. Similarly, an immune response is also involved in GVHD, but, in this case, the foreign transplanted immune cells destroy the host tissues. The  
30 administration of a polypeptide or polynucleotide of the present invention that inhibits an immune response, particularly the proliferation, differentiation, or chemotaxis of T-cells, may be an effective therapy in preventing organ rejection or GVHD.

Similarly, a polypeptide or polynucleotide of the present invention may also be used to modulate inflammation. For example, the polypeptide or polynucleotide may  
35 inhibit the proliferation and differentiation of cells involved in an inflammatory response. These molecules can be used to treat inflammatory conditions, both chronic and acute conditions, including inflammation associated with infection (e.g., septic

shock, sepsis, or systemic inflammatory response syndrome (SIRS)), ischemia-reperfusion injury, endotoxin lethality, arthritis, complement-mediated hyperacute rejection, nephritis, cytokine or chemokine induced lung injury, inflammatory bowel disease, Crohn's disease, or resulting from over production of cytokines (e.g., TNF or IL-1.)

### **Hyperproliferative Disorders**

A polypeptide or polynucleotide can be used to treat or detect hyperproliferative disorders, including neoplasms. A polypeptide or polynucleotide of the present invention may inhibit the proliferation of the disorder through direct or indirect interactions. Alternatively, a polypeptide or polynucleotide of the present invention may proliferate other cells which can inhibit the hyperproliferative disorder.

For example, by increasing an immune response, particularly increasing antigenic qualities of the hyperproliferative disorder or by proliferating, differentiating, or mobilizing T-cells, hyperproliferative disorders can be treated. This immune response may be increased by either enhancing an existing immune response, or by initiating a new immune response. Alternatively, decreasing an immune response may also be a method of treating hyperproliferative disorders, such as a chemotherapeutic agent.

Examples of hyperproliferative disorders that can be treated or detected by a polynucleotide or polypeptide of the present invention include, but are not limited to neoplasms located in the: abdomen, bone, breast, digestive system, liver, pancreas, peritoneum, endocrine glands (adrenal, parathyroid, pituitary, testicles, ovary, thymus, thyroid), eye, head and neck, nervous (central and peripheral), lymphatic system, pelvic, skin, soft tissue, spleen, thoracic, and urogenital.

Similarly, other hyperproliferative disorders can also be treated or detected by a polynucleotide or polypeptide of the present invention. Examples of such hyperproliferative disorders include, but are not limited to: hypergammaglobulinemia, lymphoproliferative disorders, paraproteinemias, purpura, sarcoidosis, Sezary Syndrome, Waldenström's Macroglobulinemia, Gaucher's Disease, histiocytosis, and any other hyperproliferative disease, besides neoplasia, located in an organ system listed above.

### **Infectious Disease**

A polypeptide or polynucleotide of the present invention can be used to treat or detect infectious agents. For example, by increasing the immune response, particularly increasing the proliferation and differentiation of B and/or T cells, infectious diseases

may be treated. The immune response may be increased by either enhancing an existing immune response, or by initiating a new immune response. Alternatively, the polypeptide or polynucleotide of the present invention may also directly inhibit the infectious agent, without necessarily eliciting an immune response.

5           Viruses are one example of an infectious agent that can cause disease or symptoms that can be treated or detected by a polynucleotide or polypeptide of the present invention. Examples of viruses, include, but are not limited to the following DNA and RNA viral families: Arbovirus, Adenoviridae, Arenaviridae, Arterivirus, Birnaviridae, Bunyaviridae, Caliciviridae, Circoviridae, Coronaviridae, Flaviviridae, Hepadnaviridae (Hepatitis), Herpesviridae (such as, Cytomegalovirus, Herpes Simplex, Herpes Zoster), Mononegavirus (e.g., Paramyxoviridae, Morbillivirus, Rhabdoviridae), Orthomyxoviridae (e.g., Influenza), Papovaviridae, Parvoviridae, Picornaviridae, Poxviridae (such as Smallpox or Vaccinia), Reoviridae (e.g., Rotavirus), Retroviridae (HTLV-I, HTLV-II, Lentivirus), and Togaviridae (e.g., Rubivirus). Viruses falling within these families can cause a variety of diseases or symptoms, including, but not limited to: arthritis, bronchiolitis, encephalitis, eye infections (e.g., conjunctivitis, keratitis), chronic fatigue syndrome, hepatitis (A, B, C, E, Chronic Active, Delta), meningitis, opportunistic infections (e.g., AIDS), pneumonia, Burkitt's Lymphoma, chickenpox, hemorrhagic fever, Measles, Mumps, Parainfluenza, Rabies, the common cold, Polio, leukemia, Rubella, sexually transmitted diseases, skin diseases (e.g., Kaposi's, warts), and viremia. A polypeptide or polynucleotide of the present invention can be used to treat or detect any of these symptoms or diseases.

25           Similarly, bacterial or fungal agents that can cause disease or symptoms and that can be treated or detected by a polynucleotide or polypeptide of the present invention include, but not limited to, the following Gram-Negative and Gram-positive bacterial families and fungi: Actinomycetales (e.g., Corynebacterium, Mycobacterium, Norcardia), Aspergillosis, Bacillaceae (e.g., Anthrax, Clostridium), Bacteroidaceae, Blastomycosis, Bordetella, Borrelia, Brucellosis, Candidiasis, Campylobacter, Coccidioidomycosis, Cryptococcosis, Dermatocycoses, Enterobacteriaceae (Klebsiella, Salmonella, Serratia, Yersinia), Erysipelothrix, Helicobacter, Legionellosis, Leptospirosis, Listeria, Mycoplasmatales, Neisseriaceae (e.g., Acinetobacter, Gonorrhea, Meningococcal), Pasteurellaceae Infections (e.g., Actinobacillus, Haemophilus, Pasteurella), Pseudomonas, Rickettsiaceae, Chlamydiaceae, Syphilis, and Staphylococcal. These bacterial or fungal families can cause the following diseases or symptoms, including, but not limited to: bacteremia, endocarditis, eye infections (conjunctivitis, tuberculosis, uveitis), gingivitis, opportunistic infections (e.g., AIDS

- related infections), paronychia, prosthesis-related infections, Reiter's Disease, respiratory tract infections, such as Whooping Cough or Empyema, sepsis, Lyme Disease, Cat-Scratch Disease, Dysentery, Paratyphoid Fever, food poisoning, Typhoid, pneumonia, Gonorrhea, meningitis, Chlamydia, Syphilis, Diphtheria,
- 5 Leprosy, Paratuberculosis, Tuberculosis, Lupus, Botulism, gangrene, tetanus, impetigo, Rheumatic Fever, Scarlet Fever, sexually transmitted diseases, skin diseases (e.g., cellulitis, dermatocycoses), toxemia, urinary tract infections, wound infections. A polypeptide or polynucleotide of the present invention can be used to treat or detect any of these symptoms or diseases.
- 10 Moreover, parasitic agents causing disease or symptoms that can be treated or detected by a polynucleotide or polypeptide of the present invention include, but not limited to, the following families: Amebiasis, Babesiosis, Coccidiosis, Cryptosporidiosis, Dientamoebiasis, Dourine, Ectoparasitic, Giardiasis, Helminthiasis, Leishmaniasis, Theileriasis, Toxoplasmosis, Trypanosomiasis, and Trichomonas.
- 15 These parasites can cause a variety of diseases or symptoms, including, but not limited to: Scabies, Trombiculiasis, eye infections, intestinal disease (e.g., dysentery, giardiasis), liver disease, lung disease, opportunistic infections (e.g., AIDS related), Malaria, pregnancy complications, and toxoplasmosis. A polypeptide or polynucleotide of the present invention can be used to treat or detect any of these symptoms or
- 20 diseases.
- Preferably, treatment using a polypeptide or polynucleotide of the present invention could either be by administering an effective amount of a polypeptide to the patient, or by removing cells from the patient, supplying the cells with a polynucleotide of the present invention, and returning the engineered cells to the patient (ex vivo
- 25 therapy). Moreover, the polypeptide or polynucleotide of the present invention can be used as an antigen in a vaccine to raise an immune response against infectious disease.

### **Regeneration**

- A polynucleotide or polypeptide of the present invention can be used to
- 30 differentiate, proliferate, and attract cells, leading to the regeneration of tissues. (See, Science 276:59-87 (1997).) The regeneration of tissues could be used to repair, replace, or protect tissue damaged by congenital defects, trauma (wounds, burns, incisions, or ulcers), age, disease (e.g. osteoporosis, osteoarthritis, periodontal disease, liver failure), surgery, including cosmetic plastic surgery, fibrosis, reperfusion
- 35 injury, or systemic cytokine damage.

Tissues that could be regenerated using the present invention include organs (e.g., pancreas, liver, intestine, kidney, skin, endothelium), muscle (smooth, skeletal

or cardiac), vascular (including vascular endothelium), nervous, hematopoietic, and skeletal (bone, cartilage, tendon, and ligament) tissue. Preferably, regeneration occurs without or decreased scarring. Regeneration also may include angiogenesis.

Moreover, a polynucleotide or polypeptide of the present invention may increase  
5 regeneration of tissues difficult to heal. For example, increased tendon/ligament regeneration would quicken recovery time after damage. A polynucleotide or polypeptide of the present invention could also be used prophylactically in an effort to avoid damage. Specific diseases that could be treated include of tendinitis, carpal tunnel syndrome, and other tendon or ligament defects. A further example of tissue  
10 regeneration of non-healing wounds includes pressure ulcers, ulcers associated with vascular insufficiency, surgical, and traumatic wounds.

Similarly, nerve and brain tissue could also be regenerated by using a polynucleotide or polypeptide of the present invention to proliferate and differentiate nerve cells. Diseases that could be treated using this method include central and  
15 peripheral nervous system diseases, neuropathies, or mechanical and traumatic disorders (e.g., spinal cord disorders, head trauma, cerebrovascular disease, and stroke). Specifically, diseases associated with peripheral nerve injuries, peripheral neuropathy (e.g., resulting from chemotherapy or other medical therapies), localized neuropathies, and central nervous system diseases (e.g., Alzheimer's disease,  
20 Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and Shy-Drager syndrome), could all be treated using the polynucleotide or polypeptide of the present invention.

### **Chemotaxis**

25 A polynucleotide or polypeptide of the present invention may have chemotaxis activity. A chemotactic molecule attracts or mobilizes cells (e.g., monocytes, fibroblasts, neutrophils, T-cells, mast cells, eosinophils, epithelial and/or endothelial cells) to a particular site in the body, such as inflammation, infection, or site of hyperproliferation. The mobilized cells can then fight off and/or heal the particular  
30 trauma or abnormality.

A polynucleotide or polypeptide of the present invention may increase chemotactic activity of particular cells. These chemotactic molecules can then be used to treat inflammation, infection, hyperproliferative disorders, or any immune system disorder by increasing the number of cells targeted to a particular location in the body.  
35 For example, chemotactic molecules can be used to treat wounds and other trauma to tissues by attracting immune cells to the injured location. Chemotactic molecules of the present invention can also attract fibroblasts, which can be used to treat wounds.



It is also contemplated that a polynucleotide or polypeptide of the present invention may inhibit chemotactic activity. These molecules could also be used to treat disorders. Thus, a polynucleotide or polypeptide of the present invention could be used as an inhibitor of chemotaxis.

5

### **Binding Activity**

A polypeptide of the present invention may be used to screen for molecules that bind to the polypeptide or for molecules to which the polypeptide binds. The binding of the polypeptide and the molecule may activate (agonist), increase, inhibit  
10 (antagonist), or decrease activity of the polypeptide or the molecule bound. Examples of such molecules include antibodies, oligonucleotides, proteins (e.g., receptors), or small molecules.

Preferably, the molecule is closely related to the natural ligand of the polypeptide, e.g., a fragment of the ligand, or a natural substrate, a ligand, a structural  
15 or functional mimetic. (See, Coligan et al., Current Protocols in Immunology 1(2):Chapter 5 (1991).) Similarly, the molecule can be closely related to the natural receptor to which the polypeptide binds, or at least, a fragment of the receptor capable of being bound by the polypeptide (e.g., active site). In either case, the molecule can be rationally designed using known techniques.

20 Preferably, the screening for these molecules involves producing appropriate cells which express the polypeptide, either as a secreted protein or on the cell membrane. Preferred cells include cells from mammals, yeast, *Drosophila*, or *E. coli*. Cells expressing the polypeptide (or cell membrane containing the expressed polypeptide) are then preferably contacted with a test compound potentially containing  
25 the molecule to observe binding, stimulation, or inhibition of activity of either the polypeptide or the molecule.

The assay may simply test binding of a candidate compound to the polypeptide, wherein binding is detected by a label, or in an assay involving competition with a labeled competitor. Further, the assay may test whether the candidate compound results  
30 in a signal generated by binding to the polypeptide.

Alternatively, the assay can be carried out using cell-free preparations, polypeptide/molecule affixed to a solid support, chemical libraries, or natural product mixtures. The assay may also simply comprise the steps of mixing a candidate compound with a solution containing a polypeptide, measuring polypeptide/molecule  
35 activity or binding, and comparing the polypeptide/molecule activity or binding to a standard.

Preferably, an ELISA assay can measure polypeptide level or activity in a sample (e.g., biological sample) using a monoclonal or polyclonal antibody. The antibody can measure polypeptide level or activity by either binding, directly or indirectly, to the polypeptide or by competing with the polypeptide for a substrate.

5 All of these above assays can be used as diagnostic or prognostic markers. The molecules discovered using these assays can be used to treat disease or to bring about a particular result in a patient (e.g., blood vessel growth) by activating or inhibiting the polypeptide/molecule. Moreover, the assays can discover agents which may inhibit or enhance the production of the polypeptide from suitably manipulated cells or tissues.

10 Therefore, the invention includes a method of identifying compounds which bind to a polypeptide of the invention comprising the steps of: (a) incubating a candidate binding compound with a polypeptide of the invention; and (b) determining if binding has occurred. Moreover, the invention includes a method of identifying agonists/antagonists comprising the steps of: (a) incubating a candidate compound with  
15 a polypeptide of the invention, (b) assaying a biological activity, and (b) determining if a biological activity of the polypeptide has been altered.

#### Other Activities

20 A polypeptide or polynucleotide of the present invention may also increase or decrease the differentiation or proliferation of embryonic stem cells, besides, as discussed above, hematopoietic lineage.

A polypeptide or polynucleotide of the present invention may also be used to modulate mammalian characteristics, such as body height, weight, hair color, eye color, skin, percentage of adipose tissue, pigmentation, size, and shape (e.g., cosmetic  
25 surgery). Similarly, a polypeptide or polynucleotide of the present invention may be used to modulate mammalian metabolism affecting catabolism, anabolism, processing, utilization, and storage of energy.

A polypeptide or polynucleotide of the present invention may be used to change a mammal's mental state or physical state by influencing biorhythms, circadian  
30 rhythms, depression (including depressive disorders), tendency for violence, tolerance for pain, reproductive capabilities (preferably by Activin or Inhibin-like activity), hormonal or endocrine levels, appetite, libido, memory, stress, or other cognitive qualities.

A polypeptide or polynucleotide of the present invention may also be used as a  
35 food additive or preservative, such as to increase or decrease storage capabilities, fat content, lipid, protein, carbohydrate, vitamins, minerals, cofactors or other nutritional components.

**Other Preferred Embodiments**

Other preferred embodiments of the claimed invention include an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least about 50 contiguous nucleotides in the nucleotide sequence of SEQ ID NO:X wherein X is any integer as defined in Table 1.

Also preferred is a nucleic acid molecule wherein said sequence of contiguous nucleotides is included in the nucleotide sequence of SEQ ID NO:X in the range of positions beginning with the nucleotide at about the position of the 5' Nucleotide of the Clone Sequence and ending with the nucleotide at about the position of the 3' Nucleotide of the Clone Sequence as defined for SEQ ID NO:X in Table 1.

Also preferred is a nucleic acid molecule wherein said sequence of contiguous nucleotides is included in the nucleotide sequence of SEQ ID NO:X in the range of positions beginning with the nucleotide at about the position of the 5' Nucleotide of the Start Codon and ending with the nucleotide at about the position of the 3' Nucleotide of the Clone Sequence as defined for SEQ ID NO:X in Table 1.

Similarly preferred is a nucleic acid molecule wherein said sequence of contiguous nucleotides is included in the nucleotide sequence of SEQ ID NO:X in the range of positions beginning with the nucleotide at about the position of the 5' Nucleotide of the First Amino Acid of the Signal Peptide and ending with the nucleotide at about the position of the 3' Nucleotide of the Clone Sequence as defined for SEQ ID NO:X in Table 1.

Also preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least about 150 contiguous nucleotides in the nucleotide sequence of SEQ ID NO:X.

Further preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least about 500 contiguous nucleotides in the nucleotide sequence of SEQ ID NO:X.

A further preferred embodiment is a nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to the nucleotide sequence of SEQ ID NO:X beginning with the nucleotide at about the position of the 5' Nucleotide of the First Amino Acid of the Signal Peptide and ending with the nucleotide at about the position of the 3' Nucleotide of the Clone Sequence as defined for SEQ ID NO:X in Table 1.

A further preferred embodiment is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to the complete nucleotide sequence of SEQ ID NO:X.

5 Also preferred is an isolated nucleic acid molecule which hybridizes under stringent hybridization conditions to a nucleic acid molecule, wherein said nucleic acid molecule which hybridizes does not hybridize under stringent hybridization conditions to a nucleic acid molecule having a nucleotide sequence consisting of only A residues or of only T residues.

10 Also preferred is a composition of matter comprising a DNA molecule which comprises a human cDNA clone identified by a cDNA Clone Identifier in Table 1, which DNA molecule is contained in the material deposited with the American Type Culture Collection and given the ATCC Deposit Number shown in Table 1 for said cDNA Clone Identifier.

15 Also preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least 50 contiguous nucleotides in the nucleotide sequence of a human cDNA clone identified by a cDNA Clone Identifier in Table 1, which DNA molecule is contained in the deposit given the ATCC Deposit Number shown in Table 1.

20 Also preferred is an isolated nucleic acid molecule, wherein said sequence of at least 50 contiguous nucleotides is included in the nucleotide sequence of the complete open reading frame sequence encoded by said human cDNA clone.

Also preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to sequence of at least 150 contiguous nucleotides in the nucleotide sequence encoded by said human cDNA clone.

25 A further preferred embodiment is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to sequence of at least 500 contiguous nucleotides in the nucleotide sequence encoded by said human cDNA clone.

A further preferred embodiment is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to the complete nucleotide  
30 sequence encoded by said human cDNA clone.

A further preferred embodiment is a method for detecting in a biological sample a nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X wherein X is any integer  
35 as defined in Table 1; and a nucleotide sequence encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1; which method

comprises a step of comparing a nucleotide sequence of at least one nucleic acid molecule in said sample with a sequence selected from said group and determining whether the sequence of said nucleic acid molecule in said sample is at least 95% identical to said selected sequence.

- 5           Also preferred is the above method wherein said step of comparing sequences comprises determining the extent of nucleic acid hybridization between nucleic acid molecules in said sample and a nucleic acid molecule comprising said sequence selected from said group. Similarly, also preferred is the above method wherein said step of comparing sequences is performed by comparing the nucleotide sequence determined  
10       from a nucleic acid molecule in said sample with said sequence selected from said group. The nucleic acid molecules can comprise DNA molecules or RNA molecules.

- A further preferred embodiment is a method for identifying the species, tissue or cell type of a biological sample which method comprises a step of detecting nucleic acid molecules in said sample, if any, comprising a nucleotide sequence that is at least 95%  
15       identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X wherein X is any integer as defined in Table 1; and a nucleotide sequence encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

- 20           The method for identifying the species, tissue or cell type of a biological sample can comprise a step of detecting nucleic acid molecules comprising a nucleotide sequence in a panel of at least two nucleotide sequences, wherein at least one sequence in said panel is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from said group.

- 25           Also preferred is a method for diagnosing in a subject a pathological condition associated with abnormal structure or expression of a gene encoding a secreted protein identified in Table 1, which method comprises a step of detecting in a biological sample obtained from said subject nucleic acid molecules, if any, comprising a nucleotide sequence that is at least 95% identical to a sequence of at least 50 contiguous  
30       nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X wherein X is any integer as defined in Table 1; and a nucleotide sequence encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

- 35           The method for diagnosing a pathological condition can comprise a step of detecting nucleic acid molecules comprising a nucleotide sequence in a panel of at least two nucleotide sequences, wherein at least one sequence in said panel is at least 95%

identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from said group.

Also preferred is a composition of matter comprising isolated nucleic acid molecules wherein the nucleotide sequences of said nucleic acid molecules comprise a panel of at least two nucleotide sequences, wherein at least one sequence in said panel is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X wherein X is any integer as defined in Table 1; and a nucleotide sequence encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1. The nucleic acid molecules can comprise DNA molecules or RNA molecules.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 90% identical to a sequence of at least about 10 contiguous amino acids in the amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1.

Also preferred is a polypeptide, wherein said sequence of contiguous amino acids is included in the amino acid sequence of SEQ ID NO:Y in the range of positions beginning with the residue at about the position of the First Amino Acid of the Secreted Portion and ending with the residue at about the Last Amino Acid of the Open Reading Frame as set forth for SEQ ID NO:Y in Table 1.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence of at least about 30 contiguous amino acids in the amino acid sequence of SEQ ID NO:Y.

Further preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence of at least about 100 contiguous amino acids in the amino acid sequence of SEQ ID NO:Y.

Further preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to the complete amino acid sequence of SEQ ID NO:Y.

Further preferred is an isolated polypeptide comprising an amino acid sequence at least 90% identical to a sequence of at least about 10 contiguous amino acids in the complete amino acid sequence of a secreted protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Also preferred is a polypeptide wherein said sequence of contiguous amino acids is included in the amino acid sequence of a secreted portion of the secreted protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence of at least about 30 contiguous amino acids in the amino acid sequence of the secreted portion of the protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence of at least about 100 contiguous amino acids in the amino acid sequence of the secreted portion of the protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to the amino acid sequence of the secreted portion of the protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Further preferred is an isolated antibody which binds specifically to a polypeptide comprising an amino acid sequence that is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1; and a complete amino acid sequence of a protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Further preferred is a method for detecting in a biological sample a polypeptide comprising an amino acid sequence which is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1; and a complete amino acid sequence of a protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1; which method comprises a step of comparing an amino acid sequence of at least one polypeptide molecule in said sample with a sequence selected from said group and determining whether the sequence of said polypeptide molecule in said sample is at least 90% identical to said sequence of at least 10 contiguous amino acids.

Also preferred is the above method wherein said step of comparing an amino acid sequence of at least one polypeptide molecule in said sample with a sequence selected from said group comprises determining the extent of specific binding of polypeptides in said sample to an antibody which binds specifically to a polypeptide

comprising an amino acid sequence that is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1; and a complete amino acid sequence of a protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Also preferred is the above method wherein said step of comparing sequences is performed by comparing the amino acid sequence determined from a polypeptide molecule in said sample with said sequence selected from said group.

Also preferred is a method for identifying the species, tissue or cell type of a biological sample which method comprises a step of detecting polypeptide molecules in said sample, if any, comprising an amino acid sequence that is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1; and a complete amino acid sequence of a secreted protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Also preferred is the above method for identifying the species, tissue or cell type of a biological sample, which method comprises a step of detecting polypeptide molecules comprising an amino acid sequence in a panel of at least two amino acid sequences, wherein at least one sequence in said panel is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the above group.

Also preferred is a method for diagnosing in a subject a pathological condition associated with abnormal structure or expression of a gene encoding a secreted protein identified in Table 1, which method comprises a step of detecting in a biological sample obtained from said subject polypeptide molecules comprising an amino acid sequence in a panel of at least two amino acid sequences, wherein at least one sequence in said panel is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1; and a complete amino acid sequence of a secreted protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

In any of these methods, the step of detecting said polypeptide molecules includes using an antibody.



Also preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a nucleotide sequence encoding a polypeptide wherein said polypeptide comprises an amino acid sequence that is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1; and a complete amino acid sequence of a secreted protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Also preferred is an isolated nucleic acid molecule, wherein said nucleotide sequence encoding a polypeptide has been optimized for expression of said polypeptide in a prokaryotic host.

Also preferred is an isolated nucleic acid molecule, wherein said polypeptide comprises an amino acid sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1; and a complete amino acid sequence of a secreted protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Further preferred is a method of making a recombinant vector comprising inserting any of the above isolated nucleic acid molecule into a vector. Also preferred is the recombinant vector produced by this method. Also preferred is a method of making a recombinant host cell comprising introducing the vector into a host cell, as well as the recombinant host cell produced by this method.

Also preferred is a method of making an isolated polypeptide comprising culturing this recombinant host cell under conditions such that said polypeptide is expressed and recovering said polypeptide. Also preferred is this method of making an isolated polypeptide, wherein said recombinant host cell is a eukaryotic cell and said polypeptide is a secreted portion of a human secreted protein comprising an amino acid sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y beginning with the residue at the position of the First Amino Acid of the Secreted Portion of SEQ ID NO:Y wherein Y is an integer set forth in Table 1 and said position of the First Amino Acid of the Secreted Portion of SEQ ID NO:Y is defined in Table 1; and an amino acid sequence of a secreted portion of a protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1. The isolated polypeptide produced by this method is also preferred.

Also preferred is a method of treatment of an individual in need of an increased level of a secreted protein activity, which method comprises administering to such an individual a pharmaceutical composition comprising an amount of an isolated polypeptide, polynucleotide, or antibody of the claimed invention effective to increase the level of said protein activity in said individual.

Having generally described the invention, the same will be more readily understood by reference to the following examples, which are provided by way of illustration and are not intended as limiting.

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### Examples

#### Example 1: Isolation of a Selected cDNA Clone From the Deposited Sample

Each cDNA clone in a cited ATCC deposit is contained in a plasmid vector. Table 1 identifies the vectors used to construct the cDNA library from which each clone was isolated. In many cases, the vector used to construct the library is a phage vector from which a plasmid has been excised. The table immediately below correlates the related plasmid for each phage vector used in constructing the cDNA library. For example, where a particular clone is identified in Table 1 as being isolated in the vector "Lambda Zap," the corresponding deposited clone is in "pBluescript."

	<u>Vector Used to Construct Library</u>	<u>Corresponding Deposited Plasmid</u>
	Lambda Zap	pBluescript (pBS)
	Uni-Zap XR	pBluescript (pBS)
	Zap Express	pBK
25	lafmid BA	plafmid BA
	pSport1	pSport1
	pCMVSPORT 2.0	pCMVSPORT 2.0
	pCMVSPORT 3.0	pCMVSPORT 3.0
	pCR <sup>®</sup> 2.1	pCR <sup>®</sup> 2.1

Vectors Lambda Zap (U.S. Patent Nos. 5,128,256 and 5,286,636), Uni-Zap XR (U.S. Patent Nos. 5,128, 256 and 5,286,636), Zap Express (U.S. Patent Nos. 5,128,256 and 5,286,636), pBluescript (pBS) (Short, J. M. et al., Nucleic Acids Res. 16:7583-7600 (1988); Altting-Mees, M. A. and Short, J. M., Nucleic Acids Res. 17:9494 (1989)) and pBK (Altting-Mees, M. A. et al., Strategies 5:58-61 (1992)) are commercially available from Stratagene Cloning Systems, Inc., 11011 N. Torrey Pines Road, La Jolla, CA, 92037. pBS contains an ampicillin resistance gene and pBK contains a neomycin resistance gene. Both can be transformed into E. coli strain XL-1

Blue, also available from Stratagene. pBS comes in 4 forms SK+, SK-, KS+ and KS. The S and K refers to the orientation of the polylinker to the T7 and T3 primer sequences which flank the polylinker region ("S" is for SacI and "K" is for KpnI which are the first sites on each respective end of the linker). "+" or "-" refer to the orientation of the f1 origin of replication ("ori"), such that in one orientation, single stranded rescue initiated from the f1 ori generates sense strand DNA and in the other, antisense.

Vectors pSport1, pCMVSPORT 2.0 and pCMVSPORT 3.0, were obtained from Life Technologies, Inc., P. O. Box 6009, Gaithersburg, MD 20897. All Sport vectors contain an ampicillin resistance gene and may be transformed into E. coli strain DH10B, also available from Life Technologies. (See, for instance, Gruber, C. E., et al., Focus 15:59 (1993).) Vector lacmid BA (Bento Soares, Columbia University, NY) contains an ampicillin resistance gene and can be transformed into E. coli strain XL-1 Blue. Vector pCR<sup>®</sup>2.1, which is available from Invitrogen, 1600 Faraday Avenue, Carlsbad, CA 92008, contains an ampicillin resistance gene and may be transformed into E. coli strain DH10B, available from Life Technologies. (See, for instance, Clark, J. M., Nuc. Acids Res. 16:9677-9686 (1988) and Mead, D. et al., Bio/Technology 9: (1991).) Preferably, a polynucleotide of the present invention does not comprise the phage vector sequences identified for the particular clone in Table 1, as well as the corresponding plasmid vector sequences designated above.

The deposited material in the sample assigned the ATCC Deposit Number cited in Table 1 for any given cDNA clone also may contain one or more additional plasmids, each comprising a cDNA clone different from that given clone. Thus, deposits sharing the same ATCC Deposit Number contain at least a plasmid for each cDNA clone identified in Table 1. Typically, each ATCC deposit sample cited in Table 1 comprises a mixture of approximately equal amounts (by weight) of about 50 plasmid DNAs, each containing a different cDNA clone; but such a deposit sample may include plasmids for more or less than 50 cDNA clones, up to about 500 cDNA clones.

Two approaches can be used to isolate a particular clone from the deposited sample of plasmid DNAs cited for that clone in Table 1. First, a plasmid is directly isolated by screening the clones using a polynucleotide probe corresponding to SEQ ID NO:X.

Particularly, a specific polynucleotide with 30-40 nucleotides is synthesized using an Applied Biosystems DNA synthesizer according to the sequence reported. The oligonucleotide is labeled, for instance, with <sup>32</sup>P-γ-ATP using T4 polynucleotide kinase and purified according to routine methods. (E.g., Maniatis et al., Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Press, Cold Spring, NY (1982).)

The plasmid mixture is transformed into a suitable host, as indicated above (such as XL-1 Blue (Stratagene)) using techniques known to those of skill in the art, such as those provided by the vector supplier or in related publications or patents cited above. The transformants are plated on 1.5% agar plates (containing the appropriate selection agent, e.g., ampicillin) to a density of about 150 transformants (colonies) per plate. These plates are screened using Nylon membranes according to routine methods for bacterial colony screening (e.g., Sambrook et al., *Molecular Cloning: A Laboratory Manual*, 2nd Edit., (1989), Cold Spring Harbor Laboratory Press, pages 1.93 to 1.104), or other techniques known to those of skill in the art.

Alternatively, two primers of 17-20 nucleotides derived from both ends of the SEQ ID NO:X (i.e., within the region of SEQ ID NO:X bounded by the 5' NT and the 3' NT of the clone defined in Table 1) are synthesized and used to amplify the desired cDNA using the deposited cDNA plasmid as a template. The polymerase chain reaction is carried out under routine conditions, for instance, in 25 µl of reaction mixture with 0.5 ug of the above cDNA template. A convenient reaction mixture is 1.5-5 mM MgCl<sub>2</sub>, 0.01% (w/v) gelatin, 20 µM each of dATP, dCTP, dGTP, dTTP, 25 pmol of each primer and 0.25 Unit of Taq polymerase. Thirty five cycles of PCR (denaturation at 94°C for 1 min; annealing at 55°C for 1 min; elongation at 72°C for 1 min) are performed with a Perkin-Elmer Cetus automated thermal cycler. The amplified product is analyzed by agarose gel electrophoresis and the DNA band with expected molecular weight is excised and purified. The PCR product is verified to be the selected sequence by subcloning and sequencing the DNA product.

Several methods are available for the identification of the 5' or 3' non-coding portions of a gene which may not be present in the deposited clone. These methods include but are not limited to, filter probing, clone enrichment using specific probes, and protocols similar or identical to 5' and 3' "RACE" protocols which are well known in the art. For instance, a method similar to 5' RACE is available for generating the missing 5' end of a desired full-length transcript. (Fromont-Racine et al., *Nucleic Acids Res.* 21(7):1683-1684 (1993).)

Briefly, a specific RNA oligonucleotide is ligated to the 5' ends of a population of RNA presumably containing full-length gene RNA transcripts. A primer set containing a primer specific to the ligated RNA oligonucleotide and a primer specific to a known sequence of the gene of interest is used to PCR amplify the 5' portion of the desired full-length gene. This amplified product may then be sequenced and used to generate the full length gene.

This above method starts with total RNA isolated from the desired source, although poly-A+ RNA can be used. The RNA preparation can then be treated with phosphatase if necessary to eliminate 5' phosphate groups on degraded or damaged RNA which may interfere with the later RNA ligase step. The phosphatase should then  
5 be inactivated and the RNA treated with tobacco acid pyrophosphatase in order to remove the cap structure present at the 5' ends of messenger RNAs. This reaction leaves a 5' phosphate group at the 5' end of the cap cleaved RNA which can then be ligated to an RNA oligonucleotide using T4 RNA ligase.

This modified RNA preparation is used as a template for first strand cDNA  
10 synthesis using a gene specific oligonucleotide. The first strand synthesis reaction is used as a template for PCR amplification of the desired 5' end using a primer specific to the ligated RNA oligonucleotide and a primer specific to the known sequence of the gene of interest. The resultant product is then sequenced and analyzed to confirm that the 5' end sequence belongs to the desired gene.

15  
**Example 2: Isolation of Genomic Clones Corresponding to a Polynucleotide**

A human genomic P1 library (Genomic Systems, Inc.) is screened by PCR  
20 using primers selected for the cDNA sequence corresponding to SEQ ID NO:X., according to the method described in Example 1. (See also, Sambrook.)

**Example 3: Tissue Distribution of Polypeptide**

Tissue distribution of mRNA expression of polynucleotides of the present invention is determined using protocols for Northern blot analysis, described by,  
25 among others, Sambrook et al. For example, a cDNA probe produced by the method described in Example 1 is labeled with P<sup>32</sup> using the rediprime™ DNA labeling system (Amersham Life Science), according to manufacturer's instructions. After labeling, the probe is purified using CHROMA SPIN-100™ column (Clontech Laboratories, Inc.), according to manufacturer's protocol number PT1200-1. The purified labeled probe is  
30 then used to examine various human tissues for mRNA expression.

Multiple Tissue Northern (MTN) blots containing various human tissues (H) or human immune system tissues (IM) (Clontech) are examined with the labeled probe using ExpressHyb™ hybridization solution (Clontech) according to manufacturer's protocol number PT1190-1. Following hybridization and washing, the blots are  
35 mounted and exposed to film at -70°C overnight, and the films developed according to standard procedures.

**Example 4: Chromosomal Mapping of the Polynucleotides**

An oligonucleotide primer set is designed according to the sequence at the 5' end of SEQ ID NO:X. This primer preferably spans about 100 nucleotides. This primer set is then used in a polymerase chain reaction under the following set of conditions : 30 seconds, 95°C; 1 minute, 56°C; 1 minute, 70°C. This cycle is repeated 32 times followed by one 5 minute cycle at 70°C. Human, mouse, and hamster DNA is used as template in addition to a somatic cell hybrid panel containing individual chromosomes or chromosome fragments (Bios, Inc). The reactions is analyzed on either 8% polyacrylamide gels or 3.5 % agarose gels. Chromosome mapping is determined by the presence of an approximately 100 bp PCR fragment in the particular somatic cell hybrid.

**Example 5: Bacterial Expression of a Polypeptide**

A polynucleotide encoding a polypeptide of the present invention is amplified using PCR oligonucleotide primers corresponding to the 5' and 3' ends of the DNA sequence, as outlined in Example 1, to synthesize insertion fragments. The primers used to amplify the cDNA insert should preferably contain restriction sites, such as BamHI and XbaI, at the 5' end of the primers in order to clone the amplified product into the expression vector. For example, BamHI and XbaI correspond to the restriction enzyme sites on the bacterial expression vector pQE-9. (Qiagen, Inc., Chatsworth, CA). This plasmid vector encodes antibiotic resistance (Amp<sup>r</sup>), a bacterial origin of replication (ori), an IPTG-regulatable promoter/operator (P/O), a ribosome binding site (RBS), a 6-histidine tag (6-His), and restriction enzyme cloning sites.

The pQE-9 vector is digested with BamHI and XbaI and the amplified fragment is ligated into the pQE-9 vector maintaining the reading frame initiated at the bacterial RBS. The ligation mixture is then used to transform the E. coli strain M15/rep4 (Qiagen, Inc.) which contains multiple copies of the plasmid pREP4, which expresses the lacI repressor and also confers kanamycin resistance (Kan<sup>r</sup>). Transformants are identified by their ability to grow on LB plates and ampicillin/kanamycin resistant colonies are selected. Plasmid DNA is isolated and confirmed by restriction analysis.

Clones containing the desired constructs are grown overnight (O/N) in liquid culture in LB media supplemented with both Amp (100 ug/ml) and Kan (25 ug/ml). The O/N culture is used to inoculate a large culture at a ratio of 1:100 to 1:250. The cells are grown to an optical density 600 (O.D.<sup>600</sup>) of between 0.4 and 0.6. IPTG

(Isopropyl-B-D-thiogalacto pyranoside) is then added to a final concentration of 1 mM. IPTG induces by inactivating the lacI repressor, clearing the P/O leading to increased gene expression.

Cells are grown for an extra 3 to 4 hours. Cells are then harvested by centrifugation (20 mins at 6000Xg). The cell pellet is solubilized in the chaotropic agent 6 Molar Guanidine HCl by stirring for 3-4 hours at 4°C. The cell debris is removed by centrifugation, and the supernatant containing the polypeptide is loaded onto a nickel-nitrilo-tri-acetic acid ("Ni-NTA") affinity resin column (available from QIAGEN, Inc., *supra*). Proteins with a 6 x His tag bind to the Ni-NTA resin with high affinity and can be purified in a simple one-step procedure (for details see: The QIAexpressionist (1995) QIAGEN, Inc., *supra*).

Briefly, the supernatant is loaded onto the column in 6 M guanidine-HCl, pH 8, the column is first washed with 10 volumes of 6 M guanidine-HCl, pH 8, then washed with 10 volumes of 6 M guanidine-HCl pH 6, and finally the polypeptide is eluted with 6 M guanidine-HCl, pH 5.

The purified protein is then renatured by dialyzing it against phosphate-buffered saline (PBS) or 50 mM Na-acetate, pH 6 buffer plus 200 mM NaCl. Alternatively, the protein can be successfully refolded while immobilized on the Ni-NTA column. The recommended conditions are as follows: renature using a linear 6M-1M urea gradient in 500 mM NaCl, 20% glycerol, 20 mM Tris/HCl pH 7.4, containing protease inhibitors. The renaturation should be performed over a period of 1.5 hours or more. After renaturation the proteins are eluted by the addition of 250 mM imidazole. Imidazole is removed by a final dialyzing step against PBS or 50 mM sodium acetate pH 6 buffer plus 200 mM NaCl. The purified protein is stored at 4°C or frozen at -80°C.

In addition to the above expression vector, the present invention further includes an expression vector comprising phage operator and promoter elements operatively linked to a polynucleotide of the present invention, called pHE4a. (ATCC Accession Number 209645, deposited on February 25, 1998.) This vector contains: 1) a neomycinphosphotransferase gene as a selection marker, 2) an E. coli origin of replication, 3) a T5 phage promoter sequence, 4) two lac operator sequences, 5) a Shine-Delgarno sequence, and 6) the lactose operon repressor gene (lacIq). The origin of replication (oriC) is derived from pUC19 (LTI, Gaithersburg, MD). The promoter sequence and operator sequences are made synthetically.

DNA can be inserted into the pHEa by restricting the vector with NdeI and XbaI, BamHI, XhoI, or Asp718, running the restricted product on a gel, and isolating the larger fragment (the stuffer fragment should be about 310 base pairs). The DNA

insert is generated according to the PCR protocol described in Example 1, using PCR primers having restriction sites for NdeI (5' primer) and XbaI, BamHI, XhoI, or Asp718 (3' primer). The PCR insert is gel purified and restricted with compatible enzymes. The insert and vector are ligated according to standard protocols.

- 5           The engineered vector could easily be substituted in the above protocol to express protein in a bacterial system.

**Example 6: Purification of a Polypeptide from an Inclusion Body**

- 10           The following alternative method can be used to purify a polypeptide expressed in *E. coli* when it is present in the form of inclusion bodies. Unless otherwise specified, all of the following steps are conducted at 4-10°C.

- Upon completion of the production phase of the *E. coli* fermentation, the cell culture is cooled to 4-10°C and the cells harvested by continuous centrifugation at 15,000 rpm (Heraeus Sepatech). On the basis of the expected yield of protein per unit weight of cell paste and the amount of purified protein required, an appropriate amount of cell paste, by weight, is suspended in a buffer solution containing 100 mM Tris, 50 mM EDTA, pH 7.4. The cells are dispersed to a homogeneous suspension using a high shear mixer.

- 20           The cells are then lysed by passing the solution through a microfluidizer (Microfluidics, Corp. or APV Gaulin, Inc.) twice at 4000-6000 psi. The homogenate is then mixed with NaCl solution to a final concentration of 0.5 M NaCl, followed by centrifugation at 7000 xg for 15 min. The resultant pellet is washed again using 0.5M NaCl, 100 mM Tris, 50 mM EDTA, pH 7.4.

- 25           The resulting washed inclusion bodies are solubilized with 1.5 M guanidine hydrochloride (GuHCl) for 2-4 hours. After 7000 xg centrifugation for 15 min., the pellet is discarded and the polypeptide containing supernatant is incubated at 4°C overnight to allow further GuHCl extraction.

- 30           Following high speed centrifugation (30,000 xg) to remove insoluble particles, the GuHCl solubilized protein is refolded by quickly mixing the GuHCl extract with 20 volumes of buffer containing 50 mM sodium, pH 4.5, 150 mM NaCl, 2 mM EDTA by vigorous stirring. The refolded diluted protein solution is kept at 4°C without mixing for 12 hours prior to further purification steps.

          To clarify the refolded polypeptide solution, a previously prepared tangential filtration unit equipped with 0.16 µm membrane filter with appropriate surface area



(e.g., Filtron), equilibrated with 40 mM sodium acetate, pH 6.0 is employed. The filtered sample is loaded onto a cation exchange resin (e.g., Poros HS-50, Perseptive Biosystems). The column is washed with 40 mM sodium acetate, pH 6.0 and eluted with 250 mM, 500 mM, 1000 mM, and 1500 mM NaCl in the same buffer, in a stepwise manner. The absorbance at 280 nm of the effluent is continuously monitored. Fractions are collected and further analyzed by SDS-PAGE.

Fractions containing the polypeptide are then pooled and mixed with 4 volumes of water. The diluted sample is then loaded onto a previously prepared set of tandem columns of strong anion (Poros HQ-50, Perseptive Biosystems) and weak anion (Poros CM-20, Perseptive Biosystems) exchange resins. The columns are equilibrated with 40 mM sodium acetate, pH 6.0. Both columns are washed with 40 mM sodium acetate, pH 6.0, 200 mM NaCl. The CM-20 column is then eluted using a 10 column volume linear gradient ranging from 0.2 M NaCl, 50 mM sodium acetate, pH 6.0 to 1.0 M NaCl, 50 mM sodium acetate, pH 6.5. Fractions are collected under constant  $A_{280}$  monitoring of the effluent. Fractions containing the polypeptide (determined, for instance, by 16% SDS-PAGE) are then pooled.

The resultant polypeptide should exhibit greater than 95% purity after the above refolding and purification steps. No major contaminant bands should be observed from Commassie blue stained 16% SDS-PAGE gel when 5  $\mu$ g of purified protein is loaded. The purified protein can also be tested for endotoxin/LPS contamination, and typically the LPS content is less than 0.1 ng/ml according to LAL assays.

#### **Example 7: Cloning and Expression of a Polypeptide in a Baculovirus Expression System**

In this example, the plasmid shuttle vector pA2 is used to insert a polynucleotide into a baculovirus to express a polypeptide. This expression vector contains the strong polyhedrin promoter of the *Autographa californica* nuclear polyhedrosis virus (AcMNPV) followed by convenient restriction sites such as BamHI, Xba I and Asp718. The polyadenylation site of the simian virus 40 ("SV40") is used for efficient polyadenylation. For easy selection of recombinant virus, the plasmid contains the beta-galactosidase gene from *E. coli* under control of a weak *Drosophila* promoter in the same orientation, followed by the polyadenylation signal of the polyhedrin gene. The inserted genes are flanked on both sides by viral sequences for cell-mediated homologous recombination with wild-type viral DNA to generate a viable virus that express the cloned polynucleotide.

Many other baculovirus vectors can be used in place of the vector above, such as pAc373, pVL941, and pAcIM1, as one skilled in the art would readily appreciate, as long as the construct provides appropriately located signals for transcription, translation, secretion and the like, including a signal peptide and an in-frame AUG as required. Such vectors are described, for instance, in Luckow et al., Virology 170:31-39 (1989).

Specifically, the cDNA sequence contained in the deposited clone, including the AUG initiation codon and the naturally associated leader sequence identified in Table 1, is amplified using the PCR protocol described in Example 1. If the naturally occurring signal sequence is used to produce the secreted protein, the pA2 vector does not need a second signal peptide. Alternatively, the vector can be modified (pA2 GP) to include a baculovirus leader sequence, using the standard methods described in Summers et al., "A Manual of Methods for Baculovirus Vectors and Insect Cell Culture Procedures," Texas Agricultural Experimental Station Bulletin No. 1555 (1987).

The amplified fragment is isolated from a 1% agarose gel using a commercially available kit ("GeneClean," BIO 101 Inc., La Jolla, Ca.). The fragment then is digested with appropriate restriction enzymes and again purified on a 1% agarose gel.

The plasmid is digested with the corresponding restriction enzymes and optionally, can be dephosphorylated using calf intestinal phosphatase, using routine procedures known in the art. The DNA is then isolated from a 1% agarose gel using a commercially available kit ("GeneClean" BIO 101 Inc., La Jolla, Ca.).

The fragment and the dephosphorylated plasmid are ligated together with T4 DNA ligase. *E. coli* HB101 or other suitable *E. coli* hosts such as XL-1 Blue (Stratagene Cloning Systems, La Jolla, CA) cells are transformed with the ligation mixture and spread on culture plates. Bacteria containing the plasmid are identified by digesting DNA from individual colonies and analyzing the digestion product by gel electrophoresis. The sequence of the cloned fragment is confirmed by DNA sequencing.

Five  $\mu$ g of a plasmid containing the polynucleotide is co-transfected with 1.0  $\mu$ g of a commercially available linearized baculovirus DNA ("BaculoGold™ baculovirus DNA", Pharmingen, San Diego, CA), using the lipofection method described by Felgner et al., Proc. Natl. Acad. Sci. USA 84:7413-7417 (1987). One  $\mu$ g of BaculoGold™ virus DNA and 5  $\mu$ g of the plasmid are mixed in a sterile well of a microtiter plate containing 50  $\mu$ l of serum-free Grace's medium (Life Technologies Inc., Gaithersburg, MD). Afterwards, 10  $\mu$ l Lipofectin plus 90  $\mu$ l Grace's medium are added, mixed and incubated for 15 minutes at room temperature. Then the transfection mixture is added drop-wise to Sf9 insect cells (ATCC CRL 1711) seeded in a 35 mm

tissue culture plate with 1 ml Grace's medium without serum. The plate is then incubated for 5 hours at 27° C. The transfection solution is then removed from the plate and 1 ml of Grace's insect medium supplemented with 10% fetal calf serum is added. Cultivation is then continued at 27° C for four days.

5        After four days the supernatant is collected and a plaque assay is performed, as described by Summers and Smith, *supra*. An agarose gel with "Blue Gal" (Life Technologies Inc., Gaithersburg) is used to allow easy identification and isolation of gal-expressing clones, which produce blue-stained plaques. (A detailed description of a "plaque assay" of this type can also be found in the user's guide for insect cell culture and baculovirology distributed by Life Technologies Inc., Gaithersburg, page 9-10.)  
10       After appropriate incubation, blue stained plaques are picked with the tip of a micropipettor (e.g., Eppendorf). The agar containing the recombinant viruses is then resuspended in a microcentrifuge tube containing 200 µl of Grace's medium and the suspension containing the recombinant baculovirus is used to infect Sf9 cells seeded in  
15       35 mm dishes. Four days later the supernatants of these culture dishes are harvested and then they are stored at 4° C.

To verify the expression of the polypeptide, Sf9 cells are grown in Grace's medium supplemented with 10% heat-inactivated FBS. The cells are infected with the recombinant baculovirus containing the polynucleotide at a multiplicity of infection  
20       ("MOI") of about 2. If radiolabeled proteins are desired, 6 hours later the medium is removed and is replaced with SF900 II medium minus methionine and cysteine (available from Life Technologies Inc., Rockville, MD). After 42 hours, 5 µCi of <sup>35</sup>S-methionine and 5 µCi <sup>35</sup>S-cysteine (available from Amersham) are added. The cells are further incubated for 16 hours and then are harvested by centrifugation. The proteins in  
25       the supernatant as well as the intracellular proteins are analyzed by SDS-PAGE followed by autoradiography (if radiolabeled).

Microsequencing of the amino acid sequence of the amino terminus of purified protein may be used to determine the amino terminal sequence of the produced protein.

#### **Example 8: Expression of a Polypeptide in Mammalian Cells**

30       The polypeptide of the present invention can be expressed in a mammalian cell. A typical mammalian expression vector contains a promoter element, which mediates the initiation of transcription of mRNA, a protein coding sequence, and signals required for the termination of transcription and polyadenylation of the transcript. Additional elements include enhancers, Kozak sequences and intervening sequences flanked by  
35       donor and acceptor sites for RNA splicing. Highly efficient transcription is achieved with the early and late promoters from SV40, the long terminal repeats (LTRs) from

Retroviruses, e.g., RSV, HTLVI, HIVI and the early promoter of the cytomegalovirus (CMV). However, cellular elements can also be used (e.g., the human actin promoter).

Suitable expression vectors for use in practicing the present invention include, for example, vectors such as pSVL and pMSG (Pharmacia, Uppsala, Sweden),  
5 pRSVcat (ATCC 37152), pSV2dhfr (ATCC 37146), pBC12MI (ATCC 67109), pCMVSPORT 2.0, and pCMVSPORT 3.0. Mammalian host cells that could be used include, human HeLa, 293, H9 and Jurkat cells, mouse NIH3T3 and C127 cells, Cos 1, Cos 7 and CV1, quail QC1-3 cells, mouse L cells and Chinese hamster ovary (CHO) cells.

10 Alternatively, the polypeptide can be expressed in stable cell lines containing the polynucleotide integrated into a chromosome. The co-transfection with a selectable marker such as dhfr, gpt, neomycin, hygromycin allows the identification and isolation of the transfected cells.

The transfected gene can also be amplified to express large amounts of the  
15 encoded protein. The DHFR (dihydrofolate reductase) marker is useful in developing cell lines that carry several hundred or even several thousand copies of the gene of interest. (See, e.g., Alt, F. W., et al., J. Biol. Chem. 253:1357-1370 (1978); Hamlin, J. L. and Ma, C., Biochem. et Biophys. Acta, 1097:107-143 (1990); Page, M. J. and Sydenham, M. A., Biotechnology 9:64-68 (1991).) Another useful selection marker is  
20 the enzyme glutamine synthase (GS) (Murphy et al., Biochem J. 227:277-279 (1991); Bebbington et al., Bio/Technology 10:169-175 (1992). Using these markers, the mammalian cells are grown in selective medium and the cells with the highest resistance are selected. These cell lines contain the amplified gene(s) integrated into a chromosome. Chinese hamster ovary (CHO) and NSO cells are often used for the  
25 production of proteins.

Derivatives of the plasmid pSV2-dhfr (ATCC Accession No. 37146), the expression vectors pC4 (ATCC Accession No. 209646) and pC6 (ATCC Accession No. 209647) contain the strong promoter (LTR) of the Rous Sarcoma Virus (Cullen et al., Molecular and Cellular Biology, 438-447 (March, 1985)) plus a fragment of the  
30 CMV-enhancer (Boshart et al., Cell 41:521-530 (1985).) Multiple cloning sites, e.g., with the restriction enzyme cleavage sites BamHI, XbaI and Asp718, facilitate the cloning of the gene of interest. The vectors also contain the 3' intron, the polyadenylation and termination signal of the rat preproinsulin gene, and the mouse DHFR gene under control of the SV40 early promoter.

35 Specifically, the plasmid pC6, for example, is digested with appropriate restriction enzymes and then dephosphorylated using calf intestinal phosphates by procedures known in the art. The vector is then isolated from a 1% agarose gel.

A polynucleotide of the present invention is amplified according to the protocol outlined in Example 1. If the naturally occurring signal sequence is used to produce the secreted protein, the vector does not need a second signal peptide. Alternatively, if the naturally occurring signal sequence is not used, the vector can be modified to include a  
5 heterologous signal sequence. (See, e.g., WO 96/34891.)

The amplified fragment is isolated from a 1% agarose gel using a commercially available kit ("Geneclean," BIO 101 Inc., La Jolla, Ca.). The fragment then is digested with appropriate restriction enzymes and again purified on a 1% agarose gel.

The amplified fragment is then digested with the same restriction enzyme and  
10 purified on a 1% agarose gel. The isolated fragment and the dephosphorylated vector are then ligated with T4 DNA ligase. *E. coli* HB101 or XL-1 Blue cells are then transformed and bacteria are identified that contain the fragment inserted into plasmid pC6 using, for instance, restriction enzyme analysis.

Chinese hamster ovary cells lacking an active DHFR gene is used for  
15 transfection. Five  $\mu$ g of the expression plasmid pC6 is cotransfected with 0.5  $\mu$ g of the plasmid pSVneo using lipofectin (Felgner et al., *supra*). The plasmid pSV2-neo contains a dominant selectable marker, the *neo* gene from Tn5 encoding an enzyme that confers resistance to a group of antibiotics including G418. The cells are seeded in alpha minus MEM supplemented with 1 mg/ml G418. After 2 days, the cells are  
20 trypsinized and seeded in hybridoma cloning plates (Greiner, Germany) in alpha minus MEM supplemented with 10, 25, or 50 ng/ml of methotrexate plus 1 mg/ml G418. After about 10-14 days single clones are trypsinized and then seeded in 6-well petri dishes or 10 ml flasks using different concentrations of methotrexate (50 nM, 100 nM, 200 nM, 400 nM, 800 nM). Clones growing at the highest concentrations of  
25 methotrexate are then transferred to new 6-well plates containing even higher concentrations of methotrexate (1  $\mu$ M, 2  $\mu$ M, 5  $\mu$ M, 10 mM, 20 mM). The same procedure is repeated until clones are obtained which grow at a concentration of 100 - 200  $\mu$ M. Expression of the desired gene product is analyzed, for instance, by SDS-PAGE and Western blot or by reversed phase HPLC analysis.

30

### **Example 9: Protein Fusions**

The polypeptides of the present invention are preferably fused to other proteins. These fusion proteins can be used for a variety of applications. For example, fusion of the present polypeptides to His-tag, HA-tag, protein A, IgG domains, and maltose  
35 binding protein facilitates purification. (See Example 5; see also EP A 394,827; Traunecker, et al., Nature 331:84-86 (1988).) Similarly, fusion to IgG-1, IgG-3, and albumin increases the halflife time in vivo. Nuclear localization signals fused to the

polypeptides of the present invention can target the protein to a specific subcellular localization, while covalent heterodimer or homodimers can increase or decrease the activity of a fusion protein. Fusion proteins can also create chimeric molecules having more than one function. Finally, fusion proteins can increase solubility and/or stability of the fused protein compared to the non-fused protein. All of the types of fusion proteins described above can be made by modifying the following protocol, which outlines the fusion of a polypeptide to an IgG molecule, or the protocol described in Example 5.

Briefly, the human Fc portion of the IgG molecule can be PCR amplified, using primers that span the 5' and 3' ends of the sequence described below. These primers also should have convenient restriction enzyme sites that will facilitate cloning into an expression vector, preferably a mammalian expression vector.

For example, if pC4 (Accession No. 209646) is used, the human Fc portion can be ligated into the BamHI cloning site. Note that the 3' BamHI site should be destroyed. Next, the vector containing the human Fc portion is re-restricted with BamHI, linearizing the vector, and a polynucleotide of the present invention, isolated by the PCR protocol described in Example 1, is ligated into this BamHI site. Note that the polynucleotide is cloned without a stop codon, otherwise a fusion protein will not be produced.

If the naturally occurring signal sequence is used to produce the secreted protein, pC4 does not need a second signal peptide. Alternatively, if the naturally occurring signal sequence is not used, the vector can be modified to include a heterologous signal sequence. (See, e.g., WO 96/34891.)

Human IgG Fc region:

```
GGGATCCGGAGCCCAAATCTTCTGACAAACTCACACATGCCCACCGTGCC
CAGCACCTGAATTCGAGGGTGCACCGTCAGTCTTCCTCTTCCCCCAAACCC
CAAGGACACCCTCATGATCTCCCGGACTCCTGAGGTCACATGCGTGGTGGT
GGACGTAAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACG
GCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAAC
AGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTG
AATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAACCCCC
ATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGT
GTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCT
GACCTGCCTGGTCAAAGGCTTCTATCCAAGCGACATCGCCGTGGAGTGGGA
GAGCAATGGGCAGCCGGAGAACAACCTACAAGACCACGCCTCCCGTGCTGG
ACTCCGACGGCTCCTTCTTCCTCTACAGCAAGCTCACCGTGGACAAGAGCA
```

GGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGC  
ACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGGTAAATGAGTGC  
GACGGCCGCGACTCTAGAGGAT (SEQ ID NO:1)

5 **Example 10: Production of an Antibody from a Polypeptide**

The antibodies of the present invention can be prepared by a variety of methods. (See, Current Protocols, Chapter 2.) For example, cells expressing a polypeptide of the present invention is administered to an animal to induce the production of sera containing polyclonal antibodies. In a preferred method, a preparation of the secreted  
10 protein is prepared and purified to render it substantially free of natural contaminants. Such a preparation is then introduced into an animal in order to produce polyclonal antisera of greater specific activity.

In the most preferred method, the antibodies of the present invention are monoclonal antibodies (or protein binding fragments thereof). Such monoclonal  
15 antibodies can be prepared using hybridoma technology. (Köhler et al., Nature 256:495 (1975); Köhler et al., Eur. J. Immunol. 6:511 (1976); Köhler et al., Eur. J. Immunol. 6:292 (1976); Hammerling et al., in: Monoclonal Antibodies and T-Cell Hybridomas, Elsevier, N.Y., pp. 563-681 (1981).) In general, such procedures involve immunizing an animal (preferably a mouse) with polypeptide or, more  
20 preferably, with a secreted polypeptide-expressing cell. Such cells may be cultured in any suitable tissue culture medium; however, it is preferable to culture cells in Earle's modified Eagle's medium supplemented with 10% fetal bovine serum (inactivated at about 56°C), and supplemented with about 10 g/l of nonessential amino acids, about 1,000 U/ml of penicillin, and about 100 µg/ml of streptomycin.

The splenocytes of such mice are extracted and fused with a suitable myeloma  
25 cell line. Any suitable myeloma cell line may be employed in accordance with the present invention; however, it is preferable to employ the parent myeloma cell line (SP2O), available from the ATCC. After fusion, the resulting hybridoma cells are selectively maintained in HAT medium, and then cloned by limiting dilution as  
30 described by Wands et al. (Gastroenterology 80:225-232 (1981).) The hybridoma cells obtained through such a selection are then assayed to identify clones which secrete antibodies capable of binding the polypeptide.

Alternatively, additional antibodies capable of binding to the polypeptide can be produced in a two-step procedure using anti-idiotypic antibodies. Such a method  
35 makes use of the fact that antibodies are themselves antigens, and therefore, it is possible to obtain an antibody which binds to a second antibody. In accordance with

this method, protein specific antibodies are used to immunize an animal, preferably a mouse. The splenocytes of such an animal are then used to produce hybridoma cells, and the hybridoma cells are screened to identify clones which produce an antibody whose ability to bind to the protein-specific antibody can be blocked by the polypeptide.

- 5 Such antibodies comprise anti-idiotypic antibodies to the protein-specific antibody and can be used to immunize an animal to induce formation of further protein-specific antibodies.

It will be appreciated that Fab and F(ab')<sub>2</sub> and other fragments of the antibodies of the present invention may be used according to the methods disclosed herein. Such  
10 fragments are typically produced by proteolytic cleavage, using enzymes such as papain (to produce Fab fragments) or pepsin (to produce F(ab')<sub>2</sub> fragments). Alternatively, secreted protein-binding fragments can be produced through the application of recombinant DNA technology or through synthetic chemistry.

- For in vivo use of antibodies in humans, it may be preferable to use  
15 "humanized" chimeric monoclonal antibodies. Such antibodies can be produced using genetic constructs derived from hybridoma cells producing the monoclonal antibodies described above. Methods for producing chimeric antibodies are known in the art. (See, for review, Morrison, Science 229:1202 (1985); Oi et al., BioTechniques 4:214 (1986); Cabilly et al., U.S. Patent No. 4,816,567; Taniguchi et al., EP 171496;  
20 Morrison et al., EP 173494; Neuberger et al., WO 8601533; Robinson et al., WO 8702671; Boulianne et al., Nature 312:643 (1984); Neuberger et al., Nature 314:268 (1985).)

#### **Example 11: Production Of Secreted Protein For High-Throughput**

##### **25 Screening Assays**

The following protocol produces a supernatant containing a polypeptide to be tested. This supernatant can then be used in the Screening Assays described in Examples 13-20.

- First, dilute Poly-D-Lysine (644 587 Boehringer-Mannheim) stock solution  
30 (1mg/ml in PBS) 1:20 in PBS (w/o calcium or magnesium 17-516F Biowhittaker) for a working solution of 50ug/ml. Add 200 ul of this solution to each well (24 well plates) and incubate at RT for 20 minutes. Be sure to distribute the solution over each well (note: a 12-channel pipetter may be used with tips on every other channel). Aspirate off the Poly-D-Lysine solution and rinse with 1ml PBS (Phosphate Buffered Saline). The  
35 PBS should remain in the well until just prior to plating the cells and plates may be poly-lysine coated in advance for up to two weeks.



Plate 293T cells (do not carry cells past P+20) at  $2 \times 10^5$  cells/well in .5ml DMEM(Dulbecco's Modified Eagle Medium)(with 4.5 G/L glucose and L-glutamine (12-604F Biowhittaker))/10% heat inactivated FBS(14-503F Biowhittaker)/1x Penstrep(17-602E Biowhittaker). Let the cells grow overnight.

- 5           The next day, mix together in a sterile solution basin: 300 ul Lipofectamine (18324-012 Gibco/BRL) and 5ml Optimem I (31985070 Gibco/BRL)/96-well plate. With a small volume multi-channel pipetter, aliquot approximately 2ug of an expression vector containing a polynucleotide insert, produced by the methods described in Examples 8 or 9, into an appropriately labeled 96-well round bottom plate. With a  
10 multi-channel pipetter, add 50ul of the Lipofectamine/Optimem I mixture to each well. Pipette up and down gently to mix. Incubate at RT 15-45 minutes. After about 20 minutes, use a multi-channel pipetter to add 150ul Optimem I to each well. As a control, one plate of vector DNA lacking an insert should be transfected with each set of transfections.

- 15           Preferably, the transfection should be performed by tag-teaming the following tasks. By tag-teaming, hands on time is cut in half, and the cells do not spend too much time on PBS. First, person A aspirates off the media from four 24-well plates of cells, and then person B rinses each well with .5-1ml PBS. Person A then aspirates off PBS rinse, and person B, using a 12-channel pipetter with tips on every other channel,  
20 adds the 200ul of DNA/Lipofectamine/Optimem I complex to the odd wells first, then to the even wells, to each row on the 24-well plates. Incubate at 37°C for 6 hours.

- While cells are incubating, prepare appropriate media, either 1%BSA in DMEM with 1x penstrep, or CHO-5 media (116.6 mg/L of  $\text{CaCl}_2$  (anhyd); 0.00130 mg/L  $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ ; 0.050 mg/L of  $\text{Fe}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$ ; 0.417 mg/L of  $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$ ; 311.80  
25 mg/L of KCl; 28.64 mg/L of  $\text{MgCl}_2$ ; 48.84 mg/L of  $\text{MgSO}_4$ ; 6995.50 mg/L of NaCl; 2400.0 mg/L of  $\text{NaHCO}_3$ ; 62.50 mg/L of  $\text{NaH}_2\text{PO}_4 \cdot \text{H}_2\text{O}$ ; 71.02 mg/L of  $\text{Na}_2\text{HPO}_4$ ; .4320 mg/L of  $\text{ZnSO}_4 \cdot 7\text{H}_2\text{O}$ ; .002 mg/L of Arachidonic Acid ; 1.022 mg/L of Cholesterol; .070 mg/L of DL-alpha-Tocopherol-Acetate; 0.0520 mg/L of Linoleic Acid; 0.010 mg/L of Linolenic Acid; 0.010 mg/L of Myristic Acid; 0.010 mg/L of Oleic  
30 Acid; 0.010 mg/L of Palmitric Acid; 0.010 mg/L of Palmitic Acid; 100 mg/L of Pluronic F-68; 0.010 mg/L of Stearic Acid; 2.20 mg/L of Tween 80; 4551 mg/L of D-Glucose; 130.85 mg/ml of L- Alanine; 147.50 mg/ml of L-Arginine-HCL; 7.50 mg/ml of L-Asparagine- $\text{H}_2\text{O}$ ; 6.65 mg/ml of L-Aspartic Acid; 29.56 mg/ml of L-Cystine-2HCL- $\text{H}_2\text{O}$ ; 31.29 mg/ml of L-Cystine-2HCL; 7.35 mg/ml of L-Glutamic Acid; 365.0  
35 mg/ml of L-Glutamine; 18.75 mg/ml of Glycine; 52.48 mg/ml of L-Histidine-HCL- $\text{H}_2\text{O}$ ; 106.97 mg/ml of L-Isoleucine; 111.45 mg/ml of L-Leucine; 163.75 mg/ml of L-

Lysine HCL; 32.34 mg/ml of L-Methionine; 68.48 mg/ml of L-Phenylalanine; 40.0 mg/ml of L-Proline; 26.25 mg/ml of L-Serine; 101.05 mg/ml of L-Threonine; 19.22 mg/ml of L-Tryptophan; 91.79 mg/ml of L-Tyrosine-2Na-2H<sub>2</sub>O; 99.65 mg/ml of L-Valine; 0.0035 mg/L of Biotin; 3.24 mg/L of D-Ca Pantothenate; 11.78 mg/L of

5 Choline Chloride; 4.65 mg/L of Folic Acid; 15.60 mg/L of i-Inositol; 3.02 mg/L of Niacinamide; 3.00 mg/L of Pyridoxal HCL; 0.031 mg/L of Pyridoxine HCL; 0.319 mg/L of Riboflavin; 3.17 mg/L of Thiamine HCL; 0.365 mg/L of Thymidine; and 0.680 mg/L of Vitamin B<sub>12</sub>; 25 mM of HEPES Buffer; 2.39 mg/L of Na Hypoxanthine; 0.105 mg/L of Lipoic Acid; 0.081 mg/L of Sodium Putrescine-2HCL; 55.0 mg/L of

10 Sodium Pyruvate; 0.0067 mg/L of Sodium Selenite; 20uM of Ethanolamine; 0.122 mg/L of Ferric Citrate; 41.70 mg/L of Methyl-B-Cyclodextrin complexed with Linoleic Acid; 33.33 mg/L of Methyl-B-Cyclodextrin complexed with Oleic Acid; and 10 mg/L of Methyl-B-Cyclodextrin complexed with Retinal) with 2mm glutamine and 1x penstrep. (BSA (81-068-3 Bayer) 100gm dissolved in 1L DMEM for a 10% BSA stock

15 solution). Filter the media and collect 50 ul for endotoxin assay in 15ml polystyrene conical.

The transfection reaction is terminated, preferably by tag-teaming, at the end of the incubation period. Person A aspirates off the transfection media, while person B adds 1.5ml appropriate media to each well. Incubate at 37°C for 45 or 72 hours

20 depending on the media used: 1%BSA for 45 hours or CHO-5 for 72 hours.

On day four, using a 300ul multichannel pipetter, aliquot 600ul in one 1ml deep well plate and the remaining supernatant into a 2ml deep well. The supernatants from each well can then be used in the assays described in Examples 13-20.

It is specifically understood that when activity is obtained in any of the assays

25 described below using a supernatant, the activity originates from either the polypeptide directly (e.g., as a secreted protein) or by the polypeptide inducing expression of other proteins, which are then secreted into the supernatant. Thus, the invention further provides a method of identifying the protein in the supernatant characterized by an activity in a particular assay.

30

#### **Example 12: Construction of GAS Reporter Construct**

One signal transduction pathway involved in the differentiation and proliferation of cells is called the Jaks-STATs pathway. Activated proteins in the Jaks-STATs pathway bind to gamma activation site "GAS" elements or interferon-sensitive

35 responsive element ("ISRE"), located in the promoter of many genes. The binding of a protein to these elements alter the expression of the associated gene.

GAS and ISRE elements are recognized by a class of transcription factors called Signal Transducers and Activators of Transcription, or "STATs." There are six members of the STATs family. Stat1 and Stat3 are present in many cell types, as is Stat2 (as response to IFN-alpha is widespread). Stat4 is more restricted and is not in many cell types though it has been found in T helper class I, cells after treatment with IL-12. Stat5 was originally called mammary growth factor, but has been found at higher concentrations in other cells including myeloid cells. It can be activated in tissue culture cells by many cytokines.

The STATs are activated to translocate from the cytoplasm to the nucleus upon tyrosine phosphorylation by a set of kinases known as the Janus Kinase ("Jaks") family. Jaks represent a distinct family of soluble tyrosine kinases and include Tyk2, Jak1, Jak2, and Jak3. These kinases display significant sequence similarity and are generally catalytically inactive in resting cells.

The Jaks are activated by a wide range of receptors summarized in the Table below. (Adapted from review by Schidler and Darnell, Ann. Rev. Biochem. 64:621-51 (1995).) A cytokine receptor family, capable of activating Jaks, is divided into two groups: (a) Class 1 includes receptors for IL-2, IL-3, IL-4, IL-6, IL-7, IL-9, IL-11, IL-12, IL-15, Epo, PRL, GH, G-CSF, GM-CSF, LIF, CNTF, and thrombopoietin; and (b) Class 2 includes IFN-a, IFN-g, and IL-10. The Class 1 receptors share a conserved cysteine motif (a set of four conserved cysteines and one tryptophan) and a WSXWS motif (a membrane proximal region encoding Trp-Ser-Xxx-Trp-Ser (SEQ ID NO:2)).

Thus, on binding of a ligand to a receptor, Jaks are activated, which in turn activate STATs, which then translocate and bind to GAS elements. This entire process is encompassed in the Jaks-STATs signal transduction pathway.

Therefore, activation of the Jaks-STATs pathway, reflected by the binding of the GAS or the ISRE element, can be used to indicate proteins involved in the proliferation and differentiation of cells. For example, growth factors and cytokines are known to activate the Jaks-STATs pathway. (See Table below.) Thus, by using GAS elements linked to reporter molecules, activators of the Jaks-STATs pathway can be identified.

	<u>Ligand</u>	<u>tyk2</u>	<u>JAKs</u> <u>Jak1</u>	<u>Jak2</u>	<u>Jak3</u>	<u>STATS</u>	<u>GAS(elements) or ISRE</u>
	<u>IFN family</u>						
5	IFN-a/B	+	+	-	-	1,2,3	ISRE
	IFN-g		+	+	-	1	GAS (IRF1>Lys6>IFP)
	Il-10	+	?	?	-	1,3	
	<u>gp130 family</u>						
10	IL-6 (Pleiotrohic)	+	+	+	?	1,3	GAS (IRF1>Lys6>IFP)
	Il-11(Pleiotrohic)	?	+	?	?	1,3	
	OnM(Pleiotrohic)	?	+	+	?	1,3	
	LIF(Pleiotrohic)	?	+	+	?	1,3	
	CNTF(Pleiotrohic)	-/+	+	+	?	1,3	
15	G-CSF(Pleiotrohic)	?	+	?	?	1,3	
	IL-12(Pleiotrohic)	+	-	+	+	1,3	
	<u>g-C family</u>						
20	IL-2 (lymphocytes)	-	+	-	+	1,3,5	GAS
	IL-4 (lymph/myeloid)	-	+	-	+	6	GAS (IRF1 = IFP >>Ly6)(IgH)
	IL-7 (lymphocytes)	-	+	-	+	5	GAS
	IL-9 (lymphocytes)	-	+	-	+	5	GAS
	IL-13 (lymphocyte)	-	+	?	?	6	GAS
	IL-15	?	+	?	+	5	GAS
25	<u>gp140 family</u>						
	IL-3 (myeloid)	-	-	+	-	5	GAS (IRF1>IFP>>Ly6)
	IL-5 (myeloid)	-	-	+	-	5	GAS
	GM-CSF (myeloid)	-	-	+	-	5	GAS
30	<u>Growth hormone family</u>						
	GH	?	-	+	-	5	
	PRL	?	+/-	+	-	1,3,5	
	EPO	?	-	+	-	5	GAS(B-CAS>IRF1=IFP>>Ly6)
35	<u>Receptor Tyrosine Kinases</u>						
	EGF	?	+	+	-	1,3	GAS (IRF1)
	PDGF	?	+	+	-	1,3	
	CSF-1	?	+	+	-	1,3	GAS (not IRF1)
40							

To construct a synthetic GAS containing promoter element, which is used in the Biological Assays described in Examples 13-14, a PCR based strategy is employed to generate a GAS-SV40 promoter sequence. The 5' primer contains four tandem copies of the GAS binding site found in the IRF1 promoter and previously demonstrated to  
5 bind STATs upon induction with a range of cytokines (Rothman et al., Immunity 1:457-468 (1994).), although other GAS or ISRE elements can be used instead. The 5' primer also contains 18bp of sequence complementary to the SV40 early promoter sequence and is flanked with an XhoI site. The sequence of the 5' primer is:  
5':GCGCCTCGAGATTTCCCCGAAATCTAGATTTCCCCGAAATGATTTCCCCG  
10 AAATGATTTCCCCGAAATATCTGCCATCTCAATTAG:3' (SEQ ID NO:3)

The downstream primer is complementary to the SV40 promoter and is flanked with a Hind III site: 5':GCGGCAAGCTTTTGGCAAAGCCTAGGC:3' (SEQ ID NO:4)

PCR amplification is performed using the SV40 promoter template present in  
15 the B-gal:promoter plasmid obtained from Clontech. The resulting PCR fragment is digested with XhoI/Hind III and subcloned into BLSK2-. (Stratagene.) Sequencing with forward and reverse primers confirms that the insert contains the following sequence:  
5':CTCGAGATTTCCCCGAAATCTAGATTTCCCCGAAATGATTTCCCCGAAATG  
20 ATTTCCCCGAAATATCTGCCATCTCAATTAGTCAGCAACCATAGTCCCGCCC  
CTAACTCCGCCCATCCCGCCCCTAACTCCGCCCAGTTCCGCCCATTCTCCGC  
CCCATGGCTGACTAATTTTTTTTATTTATGCAGAGGCCGAGGCCGCCTCGGC  
CTCTGAGCTATTCCAGAAGTAGTGAGGAGGCTTTTTTGGAGGCCTAGGCTTT  
TGCAAAAAGCTT:3' (SEQ ID NO:5)

25 With this GAS promoter element linked to the SV40 promoter, a GAS:SEAP2 reporter construct is next engineered. Here, the reporter molecule is a secreted alkaline phosphatase, or "SEAP." Clearly, however, any reporter molecule can be instead of SEAP, in this or in any of the other Examples. Well known reporter molecules that can be used instead of SEAP include chloramphenicol acetyltransferase (CAT), luciferase,  
30 alkaline phosphatase, B-galactosidase, green fluorescent protein (GFP), or any protein detectable by an antibody.

The above sequence confirmed synthetic GAS-SV40 promoter element is subcloned into the pSEAP-Promoter vector obtained from Clontech using HindIII and XhoI, effectively replacing the SV40 promoter with the amplified GAS:SV40 promoter  
35 element, to create the GAS-SEAP vector. However, this vector does not contain a neomycin resistance gene, and therefore, is not preferred for mammalian expression systems.

Thus, in order to generate mammalian stable cell lines expressing the GAS-SEAP reporter, the GAS-SEAP cassette is removed from the GAS-SEAP vector using SalI and NotI, and inserted into a backbone vector containing the neomycin resistance gene, such as pGFP-1 (Clontech), using these restriction sites in the multiple cloning site, to create the GAS-SEAP/Neo vector. Once this vector is transfected into mammalian cells, this vector can then be used as a reporter molecule for GAS binding as described in Examples 13-14.

Other constructs can be made using the above description and replacing GAS with a different promoter sequence. For example, construction of reporter molecules containing NFK-B and EGR promoter sequences are described in Examples 15 and 16. However, many other promoters can be substituted using the protocols described in these Examples. For instance, SRE, IL-2, NFAT, or Osteocalcin promoters can be substituted, alone or in combination (e.g., GAS/NF-KB/EGR, GAS/NF-KB, IL-2/NFAT, or NF-KB/GAS). Similarly, other cell lines can be used to test reporter construct activity, such as HELA (epithelial), HUVEC (endothelial), Reh (B-cell), Saos-2 (osteoblast), HUVAC (aortic), or Cardiomyocyte.

#### **Example 13: High-Throughput Screening Assay for T-cell Activity.**

The following protocol is used to assess T-cell activity by identifying factors, such as growth factors and cytokines, that may proliferate or differentiate T-cells. T-cell activity is assessed using the GAS/SEAP/Neo construct produced in Example 12. Thus, factors that increase SEAP activity indicate the ability to activate the Jaks-STATS signal transduction pathway. The T-cell used in this assay is Jurkat T-cells (ATCC Accession No. TIB-152), although Molt-3 cells (ATCC Accession No. CRL-1552) and Molt-4 cells (ATCC Accession No. CRL-1582) cells can also be used.

Jurkat T-cells are lymphoblastic CD4+ Th1 helper cells. In order to generate stable cell lines, approximately 2 million Jurkat cells are transfected with the GAS-SEAP/neo vector using DMRIE-C (Life Technologies)(transfection procedure described below). The transfected cells are seeded to a density of approximately 20,000 cells per well and transfectants resistant to 1 mg/ml gentamicin selected. Resistant colonies are expanded and then tested for their response to increasing concentrations of interferon gamma. The dose response of a selected clone is demonstrated.

Specifically, the following protocol will yield sufficient cells for 75 wells containing 200 ul of cells. Thus, it is either scaled up, or performed in multiple to generate sufficient cells for multiple 96 well plates. Jurkat cells are maintained in RPMI + 10% serum with 1%Pen-Strep. Combine 2.5 mls of OPTI-MEM (Life Technologies)

with 10 ug of plasmid DNA in a T25 flask. Add 2.5 ml OPTI-MEM containing 50 ul of DMRIE-C and incubate at room temperature for 15-45 mins.

During the incubation period, count cell concentration, spin down the required number of cells ( $10^7$  per transfection), and resuspend in OPTI-MEM to a final  
5 concentration of  $10^7$  cells/ml. Then add 1ml of  $1 \times 10^7$  cells in OPTI-MEM to T25 flask and incubate at 37°C for 6 hrs. After the incubation, add 10 ml of RPMI + 15% serum.

The Jurkat:GAS-SEAP stable reporter lines are maintained in RPMI + 10% serum, 1 mg/ml Gentamicin, and 1% Pen-Strep. These cells are treated with supernatants containing a polypeptide as produced by the protocol described in Example 11.

10 On the day of treatment with the supernatant, the cells should be washed and resuspended in fresh RPMI + 10% serum to a density of 500,000 cells per ml. The exact number of cells required will depend on the number of supernatants being screened. For one 96 well plate, approximately 10 million cells (for 10 plates, 100 million cells) are required.

15 Transfer the cells to a triangular reservoir boat, in order to dispense the cells into a 96 well dish, using a 12 channel pipette. Using a 12 channel pipette, transfer 200 ul of cells into each well (therefore adding 100, 000 cells per well).

After all the plates have been seeded, 50 ul of the supernatants are transferred directly from the 96 well plate containing the supernatants into each well using a 12  
20 channel pipette. In addition, a dose of exogenous interferon gamma (0.1, 1.0, 10 ng) is added to wells H9, H10, and H11 to serve as additional positive controls for the assay.

The 96 well dishes containing Jurkat cells treated with supernatants are placed in an incubator for 48 hrs (note: this time is variable between 48-72 hrs). 35 ul samples  
25 from each well are then transferred to an opaque 96 well plate using a 12 channel pipette. The opaque plates should be covered (using sellophene covers) and stored at -20°C until SEAP assays are performed according to Example 17. The plates containing the remaining treated cells are placed at 4°C and serve as a source of material for repeating the assay on a specific well if desired.

30 As a positive control, 100 Unit/ml interferon gamma can be used which is known to activate Jurkat T cells. Over 30 fold induction is typically observed in the positive control wells.

35 **Example 14: High-Throughput Screening Assay Identifying Myeloid Activity**

The following protocol is used to assess myeloid activity by identifying factors, such as growth factors and cytokines, that may proliferate or differentiate myeloid cells. Myeloid cell activity is assessed using the GAS/SEAP/Neo construct produced in Example 12. Thus, factors that increase SEAP activity indicate the ability to activate the Jaks-STATS signal transduction pathway. The myeloid cell used in this assay is U937, a pre-monocyte cell line, although TF-1, HL60, or KG1 can be used.

To transiently transfect U937 cells with the GAS/SEAP/Neo construct produced in Example 12, a DEAE-Dextran method (Kharbanda et. al., 1994, Cell Growth & Differentiation, 5:259-265) is used. First, harvest  $2 \times 10^7$  U937 cells and wash with PBS. The U937 cells are usually grown in RPMI 1640 medium containing 10% heat-inactivated fetal bovine serum (FBS) supplemented with 100 units/ml penicillin and 100 mg/ml streptomycin.

Next, suspend the cells in 1 ml of 20 mM Tris-HCl (pH 7.4) buffer containing 0.5 mg/ml DEAE-Dextran, 8 ug GAS-SEAP2 plasmid DNA, 140 mM NaCl, 5 mM KCl, 375 uM  $\text{Na}_2\text{HPO}_4 \cdot 7\text{H}_2\text{O}$ , 1 mM  $\text{MgCl}_2$ , and 675 uM  $\text{CaCl}_2$ . Incubate at  $37^\circ\text{C}$  for 45 min.

Wash the cells with RPMI 1640 medium containing 10% FBS and then resuspend in 10 ml complete medium and incubate at  $37^\circ\text{C}$  for 36 hr.

The GAS-SEAP/U937 stable cells are obtained by growing the cells in 400 ug/ml G418. The G418-free medium is used for routine growth but every one to two months, the cells should be re-grown in 400 ug/ml G418 for couple of passages.

These cells are tested by harvesting  $1 \times 10^8$  cells (this is enough for ten 96-well plates assay) and wash with PBS. Suspend the cells in 200 ml above described growth medium, with a final density of  $5 \times 10^5$  cells/ml. Plate 200 ul cells per well in the 96-well plate (or  $1 \times 10^5$  cells/well).

Add 50 ul of the supernatant prepared by the protocol described in Example 11. Incubate at  $37^\circ\text{C}$  for 48 to 72 hr. As a positive control, 100 Unit/ml interferon gamma can be used which is known to activate U937 cells. Over 30 fold induction is typically observed in the positive control wells. SEAP assay the supernatant according to the protocol described in Example 17.

#### **Example 15: High-Throughput Screening Assay Identifying Neuronal Activity.**

When cells undergo differentiation and proliferation, a group of genes are activated through many different signal transduction pathways. One of these genes, EGR1 (early growth response gene 1), is induced in various tissues and cell types upon



activation. The promoter of EGR1 is responsible for such induction. Using the EGR1 promoter linked to reporter molecules, activation of cells can be assessed.

Particularly, the following protocol is used to assess neuronal activity in PC12 cell lines. PC12 cells (rat phenochromocytoma cells) are known to proliferate and/or  
5 differentiate by activation with a number of mitogens, such as TPA (tetradecanoyl phorbol acetate), NGF (nerve growth factor), and EGF (epidermal growth factor). The EGR1 gene expression is activated during this treatment. Thus, by stably transfecting PC12 cells with a construct containing an EGR promoter linked to SEAP reporter, activation of PC12 cells can be assessed.

10 The EGR/SEAP reporter construct can be assembled by the following protocol. The EGR-1 promoter sequence (-633 to +1)(Sakamoto K et al., Oncogene 6:867-871 (1991)) can be PCR amplified from human genomic DNA using the following primers:

5' GCGCTCGAGGGATGACAGCGATAGAACCCCGG -3' (SEQ ID NO:6)

5' GCGAAGCTTCGCGACTCCCCGGATCCGCCTC-3' (SEQ ID NO:7)

15 Using the GAS:SEAP/Neo vector produced in Example 12, EGR1 amplified product can then be inserted into this vector. Linearize the GAS:SEAP/Neo vector using restriction enzymes XhoI/HindIII, removing the GAS/SV40 stuffer. Restrict the EGR1 amplified product with these same enzymes. Ligate the vector and the EGR1 promoter.

20 To prepare 96 well-plates for cell culture, two mls of a coating solution (1:30 dilution of collagen type I (Upstate Biotech Inc. Cat#08-115) in 30% ethanol (filter sterilized)) is added per one 10 cm plate or 50 ml per well of the 96-well plate, and allowed to air dry for 2 hr.

PC12 cells are routinely grown in RPMI-1640 medium (Bio Whittaker)  
25 containing 10% horse serum (JRH BIOSCIENCES, Cat. # 12449-78P), 5% heat-inactivated fetal bovine serum (FBS) supplemented with 100 units/ml penicillin and 100 ug/ml streptomycin on a precoated 10 cm tissue culture dish. One to four split is done every three to four days. Cells are removed from the plates by scraping and resuspended with pipetting up and down for more than 15 times.

30 Transfect the EGR/SEAP/Neo construct into PC12 using the Lipofectamine protocol described in Example 11. EGR-SEAP/PC12 stable cells are obtained by growing the cells in 300 ug/ml G418. The G418-free medium is used for routine growth but every one to two months, the cells should be re-grown in 300 ug/ml G418 for couple of passages.

35 To assay for neuronal activity, a 10 cm plate with cells around 70 to 80% confluent is screened by removing the old medium. Wash the cells once with PBS

(Phosphate buffered saline). Then starve the cells in low serum medium (RPMI-1640 containing 1% horse serum and 0.5% FBS with antibiotics) overnight.

The next morning, remove the medium and wash the cells with PBS. Scrape off the cells from the plate, suspend the cells well in 2 ml low serum medium. Count  
5 the cell number and add more low serum medium to reach final cell density as  $5 \times 10^5$  cells/ml.

Add 200 ul of the cell suspension to each well of 96-well plate (equivalent to  $1 \times 10^5$  cells/well). Add 50 ul supernatant produced by Example 11, 37°C for 48 to 72 hr. As a positive control, a growth factor known to activate PC12 cells through EGR  
10 can be used, such as 50 ng/ul of Neuronal Growth Factor (NGF). Over fifty-fold induction of SEAP is typically seen in the positive control wells. SEAP assay the supernatant according to Example 17.

**Example 16: High-Throughput Screening Assay for T-cell Activity**

15 NF- $\kappa$ B (Nuclear Factor  $\kappa$ B) is a transcription factor activated by a wide variety of agents including the inflammatory cytokines IL-1 and TNF, CD30 and CD40, lymphotoxin-alpha and lymphotoxin-beta, by exposure to LPS or thrombin, and by expression of certain viral gene products. As a transcription factor, NF- $\kappa$ B regulates the expression of genes involved in immune cell activation, control of apoptosis (NF-  
20  $\kappa$ B appears to shield cells from apoptosis), B and T-cell development, anti-viral and antimicrobial responses, and multiple stress responses.

In non-stimulated conditions, NF-  $\kappa$ B is retained in the cytoplasm with I- $\kappa$ B (Inhibitor  $\kappa$ B). However, upon stimulation, I-  $\kappa$ B is phosphorylated and degraded, causing NF-  $\kappa$ B to shuttle to the nucleus, thereby activating transcription of target  
25 genes. Target genes activated by NF-  $\kappa$ B include IL-2, IL-6, GM-CSF, ICAM-1 and class 1 MHC.

Due to its central role and ability to respond to a range of stimuli, reporter constructs utilizing the NF- $\kappa$ B promoter element are used to screen the supernatants produced in Example 11. Activators or inhibitors of NF- $\kappa$ B would be useful in treating  
30 diseases. For example, inhibitors of NF- $\kappa$ B could be used to treat those diseases related to the acute or chronic activation of NF- $\kappa$ B, such as rheumatoid arthritis.

To construct a vector containing the NF- $\kappa$ B promoter element, a PCR based strategy is employed. The upstream primer contains four tandem copies of the NF- $\kappa$ B binding site (GGGGACTTTCCC) (SEQ ID NO:8), 18 bp of sequence complementary to the 5' end of the SV40 early promoter sequence, and is flanked with an XhoI site:

5 5':GCGGCCTCGAGGGGACTTTCCCGGGGACTTTCCGGGGACTTTCCGGGAC  
TTTCCATCCTGCCATCTCAATTAG:3' (SEQ ID NO:9)

The downstream primer is complementary to the 3' end of the SV40 promoter and is flanked with a Hind III site:

5':GCGGCAAGCTTTTTGCAAAGCCTAGGC:3' (SEQ ID NO:4)

10 PCR amplification is performed using the SV40 promoter template present in the pB-gal:promoter plasmid obtained from Clontech. The resulting PCR fragment is digested with XhoI and Hind III and subcloned into BLSK2-. (Stratagene) Sequencing with the T7 and T3 primers confirms the insert contains the following sequence:

15 5':CTCGAGGGGACTTTCCCGGGGACTTTCCGGGGACTTTCCGGGACTTTCC  
ATCTGCCATCTCAATTAGTCAGCAACCATAGTCCCGCCCCTAACTCCGCCCA  
TCCCGCCCCTAACTCCGCCCCAGTTCCGCCCATTTCTCCGCCCCATGGCTGACT  
AATTTTTTTTATTTATGCAGAGGCCGAGGCCGCCTCGGCCTCTGAGCTATTC  
20 CAGAAGTAGTGAGGAGGCTTTTTTGGAGGCCTAGGCTTTTGCAAAAAGCTT:  
3' (SEQ ID NO:10)

Next, replace the SV40 minimal promoter element present in the pSEAP2- promoter plasmid (Clontech) with this NF- $\kappa$ B/SV40 fragment using XhoI and HindIII.

25 However, this vector does not contain a neomycin resistance gene, and therefore, is not preferred for mammalian expression systems.

In order to generate stable mammalian cell lines, the NF- $\kappa$ B/SV40/SEAP cassette is removed from the above NF- $\kappa$ B/SEAP vector using restriction enzymes SalI and NotI, and inserted into a vector containing neomycin resistance. Particularly, the  
30 NF- $\kappa$ B/SV40/SEAP cassette was inserted into pGFP-1 (Clontech), replacing the GFP gene, after restricting pGFP-1 with SalI and NotI.

Once NF- $\kappa$ B/SV40/SEAP/Neo vector is created, stable Jurkat T-cells are created and maintained according to the protocol described in Example 13. Similarly, the method for assaying supernatants with these stable Jurkat T-cells is also described

in Example 13. As a positive control, exogenous TNF alpha (0.1, 1, 10 ng) is added to wells H9, H10, and H11, with a 5-10 fold activation typically observed.

#### **Example 17: Assay for SEAP Activity**

- 5 As a reporter molecule for the assays described in Examples 13-16, SEAP activity is assayed using the Tropix Phospho-light Kit (Cat. BP-400) according to the following general procedure. The Tropix Phospho-light Kit supplies the Dilution, Assay, and Reaction Buffers used below.
- 10 Prime a dispenser with the 2.5x Dilution Buffer and dispense 15  $\mu$ l of 2.5x dilution buffer into Optiplates containing 35  $\mu$ l of a supernatant. Seal the plates with a plastic sealer and incubate at 65°C for 30 min. Separate the Optiplates to avoid uneven heating.
- Cool the samples to room temperature for 15 minutes. Empty the dispenser and prime with the Assay Buffer. Add 50  $\mu$ l Assay Buffer and incubate at room
- 15 temperature 5 min. Empty the dispenser and prime with the Reaction Buffer (see the table below). Add 50  $\mu$ l Reaction Buffer and incubate at room temperature for 20 minutes. Since the intensity of the chemiluminescent signal is time dependent, and it takes about 10 minutes to read 5 plates on luminometer, one should treat 5 plates at each time and start the second set 10 minutes later.
- 20 Read the relative light unit in the luminometer. Set H12 as blank, and print the results. An increase in chemiluminescence indicates reporter activity.

#### **Reaction Buffer Formulation:**

# of plates	Rxn buffer diluent (ml)	CSPD (ml)
10	60	3
11	65	3.25
12	70	3.5
13	75	3.75
14	80	4
15	85	4.25
16	90	4.5
17	95	4.75
18	100	5
19	105	5.25
20	110	5.5
21	115	5.75
22	120	6
23	125	6.25
24	130	6.5
25	135	6.75
26	140	7
27	145	7.25

28	150	7.5
29	155	7.75
30	160	8
31	165	8.25
32	170	8.5
33	175	8.75
34	180	9
35	185	9.25
36	190	9.5
37	195	9.75
38	200	10
39	205	10.25
40	210	10.5
41	215	10.75
42	220	11
43	225	11.25
44	230	11.5
45	235	11.75
46	240	12
47	245	12.25
48	250	12.5
49	255	12.75
50	260	13

**Example 18: High-Throughput Screening Assay Identifying Changes in Small Molecule Concentration and Membrane Permeability**

Binding of a ligand to a receptor is known to alter intracellular levels of small molecules, such as calcium, potassium, sodium, and pH, as well as alter membrane potential. These alterations can be measured in an assay to identify supernatants which bind to receptors of a particular cell. Although the following protocol describes an assay for calcium, this protocol can easily be modified to detect changes in potassium, sodium, pH, membrane potential, or any other small molecule which is detectable by a fluorescent probe.

The following assay uses Fluorometric Imaging Plate Reader ("FLIPR") to measure changes in fluorescent molecules (Molecular Probes) that bind small molecules. Clearly, any fluorescent molecule detecting a small molecule can be used instead of the calcium fluorescent molecule, fluo-3, used here.

For adherent cells, seed the cells at 10,000 -20,000 cells/well in a Co-star black 96-well plate with clear bottom. The plate is incubated in a CO<sub>2</sub> incubator for 20 hours. The adherent cells are washed two times in Biotek washer with 200 ul of HBSS (Hank's Balanced Salt Solution) leaving 100 ul of buffer after the final wash.

A stock solution of 1 mg/ml fluo-3 is made in 10% pluronic acid DMSO. To load the cells with fluo-3, 50 ul of 12 ug/ml fluo-3 is added to each well. The plate is

incubated at 37°C in a CO<sub>2</sub> incubator for 60 min. The plate is washed four times in the Biotek washer with HBSS leaving 100 ul of buffer.

For non-adherent cells, the cells are spun down from culture media. Cells are re-suspended to 2-5x10<sup>6</sup> cells/ml with HBSS in a 50-ml conical tube. 4 ul of 1 mg/ml fluo-3 solution in 10% pluronic acid DMSO is added to each ml of cell suspension. The tube is then placed in a 37°C water bath for 30-60 min. The cells are washed twice with HBSS, resuspended to 1x10<sup>6</sup> cells/ml, and dispensed into a microplate, 100 ul/well. The plate is centrifuged at 1000 rpm for 5 min. The plate is then washed once in Denley CellWash with 200 ul, followed by an aspiration step to 100 ul final volume.

For a non-cell based assay, each well contains a fluorescent molecule, such as fluo-3. The supernatant is added to the well, and a change in fluorescence is detected.

To measure the fluorescence of intracellular calcium, the FLIPR is set for the following parameters: (1) System gain is 300-800 mW; (2) Exposure time is 0.4 second; (3) Camera F/stop is F/2; (4) Excitation is 488 nm; (5) Emission is 530 nm; and (6) Sample addition is 50 ul. Increased emission at 530 nm indicates an extracellular signaling event which has resulted in an increase in the intracellular Ca<sup>++</sup> concentration.

#### **Example 19: High-Throughput Screening Assay Identifying Tyrosine Kinase Activity**

The Protein Tyrosine Kinases (PTK) represent a diverse group of transmembrane and cytoplasmic kinases. Within the Receptor Protein Tyrosine Kinase (RPTK) group are receptors for a range of mitogenic and metabolic growth factors including the PDGF, FGF, EGF, NGF, HGF and Insulin receptor subfamilies. In addition there are a large family of RPTKs for which the corresponding ligand is unknown. Ligands for RPTKs include mainly secreted small proteins, but also membrane-bound and extracellular matrix proteins.

Activation of RPTK by ligands involves ligand-mediated receptor dimerization, resulting in transphosphorylation of the receptor subunits and activation of the cytoplasmic tyrosine kinases. The cytoplasmic tyrosine kinases include receptor associated tyrosine kinases of the src-family (e.g., src, yes, lck, lyn, fyn) and non-receptor linked and cytosolic protein tyrosine kinases, such as the Jak family, members of which mediate signal transduction triggered by the cytokine superfamily of receptors (e.g., the Interleukins, Interferons, GM-CSF, and Leptin).

Because of the wide range of known factors capable of stimulating tyrosine kinase activity, the identification of novel human secreted proteins capable of activating

tyrosine kinase signal transduction pathways are of interest. Therefore, the following protocol is designed to identify those novel human secreted proteins capable of activating the tyrosine kinase signal transduction pathways.

Seed target cells (e.g., primary keratinocytes) at a density of approximately  
5 25,000 cells per well in a 96 well Loprodyne Silent Screen Plates purchased from  
Nalge Nunc (Naperville, IL). The plates are sterilized with two 30 minute rinses with  
100% ethanol, rinsed with water and dried overnight. Some plates are coated for 2 hr  
with 100 ml of cell culture grade type I collagen (50 mg/ml), gelatin (2%) or polylysine  
(50 mg/ml), all of which can be purchased from Sigma Chemicals (St. Louis, MO) or  
10 10% Matrigel purchased from Becton Dickinson (Bedford, MA), or calf serum, rinsed  
with PBS and stored at 4°C. Cell growth on these plates is assayed by seeding 5,000  
cells/well in growth medium and indirect quantitation of cell number through use of  
AlamarBlue as described by the manufacturer Alamar Biosciences, Inc. (Sacramento,  
CA) after 48 hr. Falcon plate covers #3071 from Becton Dickinson (Bedford, MA) are  
15 used to cover the Loprodyne Silent Screen Plates. Falcon Microtest III cell culture  
plates can also be used in some proliferation experiments.

To prepare extracts, A431 cells are seeded onto the nylon membranes of  
Loprodyne plates (20,000/200ml/well) and cultured overnight in complete medium.  
Cells are quiesced by incubation in serum-free basal medium for 24 hr. After 5-20  
20 minutes treatment with EGF (60ng/ml) or 50 ul of the supernatant produced in Example  
11, the medium was removed and 100 ml of extraction buffer ((20 mM HEPES pH  
7.5, 0.15 M NaCl, 1% Triton X-100, 0.1% SDS, 2 mM Na<sub>3</sub>VO<sub>4</sub>, 2 mM Na<sub>4</sub>P<sub>2</sub>O<sub>7</sub>  
and a cocktail of protease inhibitors (# 1836170) obtained from Boehringer Mannheim  
(Indianapolis, IN) is added to each well and the plate is shaken on a rotating shaker for  
25 5 minutes at 4°C. The plate is then placed in a vacuum transfer manifold and the extract  
filtered through the 0.45 mm membrane bottoms of each well using house vacuum.  
Extracts are collected in a 96-well catch/assay plate in the bottom of the vacuum  
manifold and immediately placed on ice. To obtain extracts clarified by centrifugation,  
the content of each well, after detergent solubilization for 5 minutes, is removed and  
30 centrifuged for 15 minutes at 4°C at 16,000 x g.

Test the filtered extracts for levels of tyrosine kinase activity. Although many  
methods of detecting tyrosine kinase activity are known, one method is described here.

Generally, the tyrosine kinase activity of a supernatant is evaluated by  
determining its ability to phosphorylate a tyrosine residue on a specific substrate (a  
35 biotinylated peptide). Biotinylated peptides that can be used for this purpose include  
PSK1 (corresponding to amino acids 6-20 of the cell division kinase cdc2-p34) and

PSK2 (corresponding to amino acids 1-17 of gastrin). Both peptides are substrates for a range of tyrosine kinases and are available from Boehringer Mannheim.

The tyrosine kinase reaction is set up by adding the following components in order. First, add 10ul of 5uM Biotinylated Peptide, then 10ul ATP/Mg<sub>2</sub><sup>+</sup> (5mM  
5 ATP/50mM MgCl<sub>2</sub>), then 10ul of 5x Assay Buffer (40mM imidazole hydrochloride, pH7.3, 40 mM beta-glycerophosphate, 1mM EGTA, 100mM MgCl<sub>2</sub>, 5 mM MnCl<sub>2</sub>, 0.5 mg/ml BSA), then 5ul of Sodium Vanadate(1mM), and then 5ul of water. Mix the components gently and preincubate the reaction mix at 30°C for 2 min. Initial the reaction by adding 10ul of the control enzyme or the filtered supernatant.

10 The tyrosine kinase assay reaction is then terminated by adding 10 ul of 120mM EDTA and place the reactions on ice.

Tyrosine kinase activity is determined by transferring 50 ul aliquot of reaction mixture to a microtiter plate (MTP) module and incubating at 37°C for 20 min. This allows the streptavidin coated 96 well plate to associate with the biotinylated peptide.  
15 Wash the MTP module with 300ul/well of PBS four times. Next add 75 ul of anti-phosphotyrosine antibody conjugated to horse radish peroxidase(anti-P-Tyr-POD(0.5u/ml)) to each well and incubate at 37°C for one hour. Wash the well as above.

Next add 100ul of peroxidase substrate solution (Boehringer Mannheim) and  
20 incubate at room temperature for at least 5 mins (up to 30 min). Measure the absorbance of the sample at 405 nm by using ELISA reader. The level of bound peroxidase activity is quantitated using an ELISA reader and reflects the level of tyrosine kinase activity.

#### 25 **Example 20: High-Throughput Screening Assay Identifying Phosphorylation Activity**

As a potential alternative and/or compliment to the assay of protein tyrosine kinase activity described in Example 19, an assay which detects activation (phosphorylation) of major intracellular signal transduction intermediates can also be  
30 used. For example, as described below one particular assay can detect tyrosine phosphorylation of the Erk-1 and Erk-2 kinases. However, phosphorylation of other molecules, such as Raf, JNK, p38 MAP, Map kinase kinase (MEK), MEK kinase, Src, Muscle specific kinase (MuSK), IRAK, Tec, and Janus, as well as any other phosphoserine, phosphotyrosine, or phosphothreonine molecule, can be detected by  
35 substituting these molecules for Erk-1 or Erk-2 in the following assay.



Specifically, assay plates are made by coating the wells of a 96-well ELISA plate with 0.1ml of protein G (1ug/ml) for 2 hr at room temp, (RT). The plates are then rinsed with PBS and blocked with 3% BSA/PBS for 1 hr at RT. The protein G plates are then treated with 2 commercial monoclonal antibodies (100ng/well) against Erk-1 and Erk-2 (1 hr at RT) (Santa Cruz Biotechnology). (To detect other molecules, this step can easily be modified by substituting a monoclonal antibody detecting any of the above described molecules.) After 3-5 rinses with PBS, the plates are stored at 4°C until use.

A431 cells are seeded at 20,000/well in a 96-well Loprodyne filterplate and cultured overnight in growth medium. The cells are then starved for 48 hr in basal medium (DMEM) and then treated with EGF (6ng/well) or 50 ul of the supernatants obtained in Example 11 for 5-20 minutes. The cells are then solubilized and extracts filtered directly into the assay plate.

After incubation with the extract for 1 hr at RT, the wells are again rinsed. As a positive control, a commercial preparation of MAP kinase (10ng/well) is used in place of A431 extract. Plates are then treated with a commercial polyclonal (rabbit) antibody (1ug/ml) which specifically recognizes the phosphorylated epitope of the Erk-1 and Erk-2 kinases (1 hr at RT). This antibody is biotinylated by standard procedures. The bound polyclonal antibody is then quantitated by successive incubations with Europium-streptavidin and Europium fluorescence enhancing reagent in the Wallac DELFIA instrument (time-resolved fluorescence). An increased fluorescent signal over background indicates a phosphorylation.

**Example 21: Method of Determining Alterations in a Gene**  
**Corresponding to a Polynucleotide**

RNA isolated from entire families or individual patients presenting with a phenotype of interest (such as a disease) is be isolated. cDNA is then generated from these RNA samples using protocols known in the art. (See, Sambrook.) The cDNA is then used as a template for PCR, employing primers surrounding regions of interest in SEQ ID NO:X. Suggested PCR conditions consist of 35 cycles at 95°C for 30 seconds; 60-120 seconds at 52-58°C; and 60-120 seconds at 70°C, using buffer solutions described in Sidransky, D., et al., Science 252:706 (1991).

PCR products are then sequenced using primers labeled at their 5' end with T4 polynucleotide kinase, employing SequiTherm Polymerase. (Epicentre Technologies). The intron-exon borders of selected exons is also determined and genomic PCR

products analyzed to confirm the results. PCR products harboring suspected mutations is then cloned and sequenced to validate the results of the direct sequencing.

PCR products is cloned into T-tailed vectors as described in Holton, T.A. and Graham, M.W., Nucleic Acids Research, 19:1156 (1991) and sequenced with T7  
5 polymerase (United States Biochemical). Affected individuals are identified by mutations not present in unaffected individuals.

Genomic rearrangements are also observed as a method of determining alterations in a gene corresponding to a polynucleotide. Genomic clones isolated according to Example 2 are nick-translated with digoxigenindeoxy-uridine 5'-  
10 triphosphate (Boehringer Mannheim), and FISH performed as described in Johnson, Cg. et al., Methods Cell Biol. 35:73-99 (1991). Hybridization with the labeled probe is carried out using a vast excess of human cot-1 DNA for specific hybridization to the corresponding genomic locus.

Chromosomes are counterstained with 4,6-diamino-2-phenylidole and  
15 propidium iodide, producing a combination of C- and R-bands. Aligned images for precise mapping are obtained using a triple-band filter set (Chroma Technology, Brattleboro, VT) in combination with a cooled charge-coupled device camera (Photometrics, Tucson, AZ) and variable excitation wavelength filters. (Johnson, Cv. et al., Genet. Anal. Tech. Appl., 8:75 (1991).) Image collection, analysis and  
20 chromosomal fractional length measurements are performed using the ISee Graphical Program System. (Inovision Corporation, Durham, NC.) Chromosome alterations of the genomic region hybridized by the probe are identified as insertions, deletions, and translocations. These alterations are used as a diagnostic marker for an associated disease.

25

**Example 22: Method of Detecting Abnormal Levels of a Polypeptide in a Biological Sample**

A polypeptide of the present invention can be detected in a biological sample, and if an increased or decreased level of the polypeptide is detected, this polypeptide is  
30 a marker for a particular phenotype. Methods of detection are numerous, and thus, it is understood that one skilled in the art can modify the following assay to fit their particular needs.

For example, antibody-sandwich ELISAs are used to detect polypeptides in a sample, preferably a biological sample. Wells of a microtiter plate are coated with  
35 specific antibodies, at a final concentration of 0.2 to 10 ug/ml. The antibodies are either monoclonal or polyclonal and are produced by the method described in Example 10.

The wells are blocked so that non-specific binding of the polypeptide to the well is reduced.

The coated wells are then incubated for > 2 hours at RT with a sample containing the polypeptide. Preferably, serial dilutions of the sample should be used to validate results. The plates are then washed three times with deionized or distilled water to remove unbounded polypeptide.

Next, 50 ul of specific antibody-alkaline phosphatase conjugate, at a concentration of 25-400 ng, is added and incubated for 2 hours at room temperature. The plates are again washed three times with deionized or distilled water to remove unbounded conjugate.

Add 75 ul of 4-methylumbelliferyl phosphate (MUP) or p-nitrophenyl phosphate (NPP) substrate solution to each well and incubate 1 hour at room temperature. Measure the reaction by a microtiter plate reader. Prepare a standard curve, using serial dilutions of a control sample, and plot polypeptide concentration on the X-axis (log scale) and fluorescence or absorbance of the Y-axis (linear scale). Interpolate the concentration of the polypeptide in the sample using the standard curve.

### **Example 23: Formulating a Polypeptide**

The secreted polypeptide composition will be formulated and dosed in a fashion consistent with good medical practice, taking into account the clinical condition of the individual patient (especially the side effects of treatment with the secreted polypeptide alone), the site of delivery, the method of administration, the scheduling of administration, and other factors known to practitioners. The "effective amount" for purposes herein is thus determined by such considerations.

As a general proposition, the total pharmaceutically effective amount of secreted polypeptide administered parenterally per dose will be in the range of about 1 µg/kg/day to 10 mg/kg/day of patient body weight, although, as noted above, this will be subject to therapeutic discretion. More preferably, this dose is at least 0.01 mg/kg/day, and most preferably for humans between about 0.01 and 1 mg/kg/day for the hormone. If given continuously, the secreted polypeptide is typically administered at a dose rate of about 1 µg/kg/hour to about 50 µg/kg/hour, either by 1-4 injections per day or by continuous subcutaneous infusions, for example, using a mini-pump. An intravenous bag solution may also be employed. The length of treatment needed to observe changes and the interval following treatment for responses to occur appears to vary depending on the desired effect.

Pharmaceutical compositions containing the secreted protein of the invention are administered orally, rectally, parenterally, intracisternally, intravaginally,

intraperitoneally, topically (as by powders, ointments, gels, drops or transdermal patch), buccally, or as an oral or nasal spray. "Pharmaceutically acceptable carrier" refers to a non-toxic solid, semisolid or liquid filler, diluent, encapsulating material or formulation auxiliary of any type. The term "parenteral" as used herein refers to modes of administration which include intravenous, intramuscular, intraperitoneal, intrasternal, subcutaneous and intraarticular injection and infusion.

The secreted polypeptide is also suitably administered by sustained-release systems. Suitable examples of sustained-release compositions include semi-permeable polymer matrices in the form of shaped articles, e.g., films, or microcapsules.

Sustained-release matrices include polylactides (U.S. Pat. No. 3,773,919, EP 58,481), copolymers of L-glutamic acid and gamma-ethyl-L-glutamate (Sidman, U. et al., Biopolymers 22:547-556 (1983)), poly (2- hydroxyethyl methacrylate) (R. Langer et al., J. Biomed. Mater. Res. 15:167-277 (1981), and R. Langer, Chem. Tech. 12:98-105 (1982)), ethylene vinyl acetate (R. Langer et al.) or poly-D- (-)-3-hydroxybutyric acid (EP 133,988). Sustained-release compositions also include liposomally entrapped polypeptides. Liposomes containing the secreted polypeptide are prepared by methods known per se: DE 3,218,121; Epstein et al., Proc. Natl. Acad. Sci. USA 82:3688-3692 (1985); Hwang et al., Proc. Natl. Acad. Sci. USA 77:4030-4034 (1980); EP 52,322; EP 36,676; EP 88,046; EP 143,949; EP 142,641; Japanese Pat. Appl. 83-118008; U.S. Pat. Nos. 4,485,045 and 4,544,545; and EP 102,324. Ordinarily, the liposomes are of the small (about 200-800 Angstroms) unilamellar type in which the lipid content is greater than about 30 mol. percent cholesterol, the selected proportion being adjusted for the optimal secreted polypeptide therapy.

For parenteral administration, in one embodiment, the secreted polypeptide is formulated generally by mixing it at the desired degree of purity, in a unit dosage injectable form (solution, suspension, or emulsion), with a pharmaceutically acceptable carrier, i.e., one that is non-toxic to recipients at the dosages and concentrations employed and is compatible with other ingredients of the formulation. For example, the formulation preferably does not include oxidizing agents and other compounds that are known to be deleterious to polypeptides.

Generally, the formulations are prepared by contacting the polypeptide uniformly and intimately with liquid carriers or finely divided solid carriers or both. Then, if necessary, the product is shaped into the desired formulation. Preferably the carrier is a parenteral carrier, more preferably a solution that is isotonic with the blood of the recipient. Examples of such carrier vehicles include water, saline, Ringer's solution, and dextrose solution. Non-aqueous vehicles such as fixed oils and ethyl oleate are also useful herein, as well as liposomes.

The carrier suitably contains minor amounts of additives such as substances that enhance isotonicity and chemical stability. Such materials are non-toxic to recipients at the dosages and concentrations employed, and include buffers such as phosphate, citrate, succinate, acetic acid, and other organic acids or their salts; antioxidants such as ascorbic acid; low molecular weight (less than about ten residues) polypeptides, e.g., polyarginine or tripeptides; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids, such as glycine, glutamic acid, aspartic acid, or arginine; monosaccharides, disaccharides, and other carbohydrates including cellulose or its derivatives, glucose, manose, or dextrans; chelating agents such as EDTA; sugar alcohols such as mannitol or sorbitol; counterions such as sodium; and/or nonionic surfactants such as polysorbates, poloxamers, or PEG.

The secreted polypeptide is typically formulated in such vehicles at a concentration of about 0.1 mg/ml to 100 mg/ml, preferably 1-10 mg/ml, at a pH of about 3 to 8. It will be understood that the use of certain of the foregoing excipients, carriers, or stabilizers will result in the formation of polypeptide salts.

Any polypeptide to be used for therapeutic administration can be sterile. Sterility is readily accomplished by filtration through sterile filtration membranes (e.g., 0.2 micron membranes). Therapeutic polypeptide compositions generally are placed into a container having a sterile access port, for example, an intravenous solution bag or vial having a stopper pierceable by a hypodermic injection needle.

Polypeptides ordinarily will be stored in unit or multi-dose containers, for example, sealed ampoules or vials, as an aqueous solution or as a lyophilized formulation for reconstitution. As an example of a lyophilized formulation, 10-ml vials are filled with 5 ml of sterile-filtered 1% (w/v) aqueous polypeptide solution, and the resulting mixture is lyophilized. The infusion solution is prepared by reconstituting the lyophilized polypeptide using bacteriostatic Water-for-Injection.

The invention also provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical compositions of the invention. Associated with such container(s) can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration. In addition, the polypeptides of the present invention may be employed in conjunction with other therapeutic compounds.

35

**Example 24: Method of Treating Decreased Levels of the Polypeptide**

pMV-7 (Kirschmeier, P.T. et al., DNA, 7:219-25 (1988)), flanked by the long terminal repeats of the Moloney murine sarcoma virus, is digested with EcoRI and HindIII and subsequently treated with calf intestinal phosphatase. The linear vector is fractionated on agarose gel and purified, using glass beads.

5       The cDNA encoding a polypeptide of the present invention can be amplified using PCR primers which correspond to the 5' and 3' end sequences respectively as set forth in Example 1. Preferably, the 5' primer contains an EcoRI site and the 3' primer includes a HindIII site. Equal quantities of the Moloney murine sarcoma virus linear backbone and the amplified EcoRI and HindIII fragment are added together, in the  
10       presence of T4 DNA ligase. The resulting mixture is maintained under conditions appropriate for ligation of the two fragments. The ligation mixture is then used to transform bacteria HB101, which are then plated onto agar containing kanamycin for the purpose of confirming that the vector has the gene of interest properly inserted.

15       The amphotropic pA317 or GP+am12 packaging cells are grown in tissue culture to confluent density in Dulbecco's Modified Eagles Medium (DMEM) with 10% calf serum (CS), penicillin and streptomycin. The MSV vector containing the gene is then added to the media and the packaging cells transduced with the vector. The packaging cells now produce infectious viral particles containing the gene (the packaging cells are now referred to as producer cells).

20       Fresh media is added to the transduced producer cells, and subsequently, the media is harvested from a 10 cm plate of confluent producer cells. The spent media, containing the infectious viral particles, is filtered through a millipore filter to remove detached producer cells and this media is then used to infect fibroblast cells. Media is removed from a sub-confluent plate of fibroblasts and quickly replaced with the media  
25       from the producer cells. This media is removed and replaced with fresh media. If the titer of virus is high, then virtually all fibroblasts will be infected and no selection is required. If the titer is very low, then it is necessary to use a retroviral vector that has a selectable marker, such as neo or his. Once the fibroblasts have been efficiently infected, the fibroblasts are analyzed to determine whether protein is produced.

30       The engineered fibroblasts are then transplanted onto the host, either alone or after having been grown to confluence on cytodex 3 microcarrier beads.

#### **Example 27: Method of Treatment Using Gene Therapy - In Vivo**

35       Another aspect of the present invention is using *in vivo* gene therapy methods to treat disorders, diseases and conditions. The gene therapy method relates to the introduction of naked nucleic acid (DNA, RNA, and antisense DNA or RNA) sequences into an animal to increase or decrease the expression

of the polypeptide of the present invention. A polynucleotide of the present invention may be operatively linked to a promoter or any other genetic elements necessary for the expression of the encoded polypeptide by the target tissue. Such gene therapy and delivery techniques and methods are known in the art, see, for example, WO90/11092, WO98/11779; U.S. Patent NO. 5693622, 5705151, 5580859; Tabata H. et al. (1997) *Cardiovasc. Res.* 35(3):470-479, Chao J et al. (1997) *Pharmacol. Res.* 35(6):517-522, Wolff J.A. (1997) *Neuromuscul. Disord.* 7(5):314-318, Schwartz B. et al. (1996) *Gene Ther.* 3(5):405-411, Tsurumi Y. et al. (1996) *Circulation* 94(12):3281-3290 (incorporated herein by reference).

The polynucleotide constructs of the present invention may be delivered by any method that delivers injectable materials to the cells of an animal, such as, injection into the interstitial space of tissues (heart, muscle, skin, lung, liver, intestine and the like). These polynucleotide constructs can be delivered in a pharmaceutically acceptable liquid or aqueous carrier.

The term "naked" polynucleotide, DNA or RNA, refers to sequences that are free from any delivery vehicle that acts to assist, promote, or facilitate entry into the cell, including viral sequences, viral particles, liposome formulations, lipofectin or precipitating agents and the like. However, the polynucleotides may also be delivered in liposome formulations (such as those taught in Felgner P.L. et al. (1995) *Ann. NY Acad. Sci.* 772:126-139 and Abdallah B. et al. (1995) *Biol. Cell* 85(1):1-7) which can be prepared by methods well known to those skilled in the art.

The polynucleotide vector constructs of the present invention used in the gene therapy method are preferably constructs that will not integrate into the host genome nor will they contain sequences that allow for replication. Any strong promoter known to those skilled in the art can be used for driving the expression of DNA. Unlike other gene therapies techniques, one major advantage of introducing naked nucleic acid sequences into target cells is the transitory nature of the polynucleotide synthesis in the cells. Studies have shown that non-replicating DNA sequences can be introduced into cells to provide production of the desired polypeptide for periods of up to six months.

The polynucleotide construct of the present invention can be delivered to the interstitial space of tissues within the an animal, including of muscle, skin, brain, lung, liver, spleen, bone marrow, thymus, heart, lymph, blood, bone, cartilage, pancreas, kidney, gall bladder, stomach, intestine, testis, ovary, uterus, rectum, nervous system, eye, gland, and connective tissue. Interstitial

space of the tissues comprises the intercellular fluid, mucopolysaccharide matrix among the reticular fibers of organ tissues, elastic fibers in the walls of vessels or chambers, collagen fibers of fibrous tissues, or that same matrix within connective tissue ensheathing muscle cells or in the lacunae of bone. It is similarly the space occupied by the plasma of the circulation and the lymph fluid of the lymphatic channels. Delivery to the interstitial space of muscle tissue is preferred for the reasons discussed below. They may be conveniently delivered by injection into the tissues comprising these cells. They are preferably delivered to and expressed in persistent, non-dividing cells which are differentiated, although delivery and expression may be achieved in non-differentiated or less completely differentiated cells, such as, for example, stem cells of blood or skin fibroblasts. *In vivo* muscle cells are particularly competent in their ability to take up and express polynucleotides.

For the naked polynucleotide injection, an effective dosage amount of DNA or RNA will be in the range of from about 0.05 g/kg body weight to about 50 mg/kg body weight. Preferably the dosage will be from about 0.005 mg/kg to about 20 mg/kg and more preferably from about 0.05 mg/kg to about 5 mg/kg. Of course, as the artisan of ordinary skill will appreciate, this dosage will vary according to the tissue site of injection. The appropriate and effective dosage of nucleic acid sequence can readily be determined by those of ordinary skill in the art and may depend on the condition being treated and the route of administration. The preferred route of administration is by the parenteral route of injection into the interstitial space of tissues. However, other parenteral routes may also be used, such as, inhalation of an aerosol formulation particularly for delivery to lungs or bronchial tissues, throat or mucous membranes of the nose. In addition, naked polynucleotide constructs can be delivered to arteries during angioplasty by the catheter used in the procedure.

The dose response effects of injected polynucleotide in muscle *in vivo* is determined as follows. Suitable template DNA for production of mRNA coding for the polypeptide of the present invention is prepared in accordance with a standard recombinant DNA methodology. The template DNA, which may be either circular or linear, is either used as naked DNA or complexed with liposomes. The quadriceps muscles of mice are then injected with various amounts of the template DNA.

Five to six week old female and male Balb/C mice are anesthetized by intraperitoneal injection with 0.3 ml of 2.5% Avertin. A 1.5 cm incision is made on the anterior thigh, and the quadriceps muscle is directly visualized. The



template DNA is injected in 0.1 ml of carrier in a 1 cc syringe through a 27 gauge needle over one minute, approximately 0.5 cm from the distal insertion site of the muscle into the knee and about 0.2 cm deep. A suture is placed over the injection site for future localization, and the skin is closed with stainless steel clips.

After an appropriate incubation time (e.g., 7 days) muscle extracts are prepared by excising the entire quadriceps. Every fifth 15 um cross-section of the individual quadriceps muscles is histochemically stained for protein expression. A time course for protein expression may be done in a similar fashion except that quadriceps from different mice are harvested at different times. Persistence of DNA in muscle following injection may be determined by Southern blot analysis after preparing total cellular DNA and HIRT supernatants from injected and control mice. The results of the above experimentation in mice can be use to extrapolate proper dosages and other treatment parameters in humans and other animals using naked DNA of the present invention.

It will be clear that the invention may be practiced otherwise than as particularly described in the foregoing description and examples. Numerous modifications and variations of the present invention are possible in light of the above teachings and, therefore, are within the scope of the appended claims.


The entire disclosure of each document cited (including patents, patent applications, journal articles, abstracts, laboratory manuals, books, or other disclosures) in the Background of the Invention, Detailed Description, and Examples is hereby incorporated herein by reference.

Further, the Sequence Listing submitted herewith in paper and computer readable forms are herein incorporated by reference in their entireties.

## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM


(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>143</u> , line <u>N/A</u>	
<b>B. IDENTIFICATION OF DEPOSIT</b> Further deposits are identified on an additional sheet	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America	
Date of deposit June 12, 1997	Accession Number 209119
<b>C. ADDITIONAL INDICATIONS</b> (leave blank if not applicable) This information is continued on an additional sheet	
<b>D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE</b> (if the indications are not for all designated States)	
<b>E. SEPARATE FURNISHING OF INDICATIONS</b> (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")	

<b>For receiving Office use only</b>	<b>For International Bureau use only</b>
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(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>145</u> , line <u>N/A</u>	
<b>B. IDENTIFICATION OF DEPOSIT</b> Further deposits are identified on an additional sheet <input type="checkbox"/>	
Name of depositary institution American Type Culture Collection	
Address of depositary institution (including postal code and country) 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America	
Date of deposit June 19, 1997	Accession Number 209124
<b>C. ADDITIONAL INDICATIONS</b> (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
<b>D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE</b> (if the indications are not for all designated States)	
<b>E. SEPARATE FURNISHING OF INDICATIONS</b> (leave blank if not applicable) The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")	
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## INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

<b>A.</b> The indications made below relate to the microorganism referred to in the description on page <u>148</u> , line <u>N/A</u>	
<b>B. IDENTIFICATION OF DEPOSIT</b> <span style="float: right;">Further deposits are identified on an additional sheet <input type="checkbox"/></span>	
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Address of depositary institution (including postal code and country) 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America	
Date of deposit    June 19, 1997	Accession Number    209125
<b>C. ADDITIONAL INDICATIONS</b> (leave blank if not applicable) <span style="float: right;">This information is continued on an additional sheet <input type="checkbox"/></span>	
<b>D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE</b> (if the indications are not for all designated States)	
<b>E. SEPARATE FURNISHING OF INDICATIONS</b> (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit")	

<div style="text-align: center;">For receiving Office use only</div> <div style="border: 1px solid black; padding: 5px; margin-top: 10px;"><input checked="" type="checkbox"/> This sheet was received with the international application</div> <div style="border: 1px solid black; padding: 5px; margin-top: 10px;">Authorized officer </div>	<div style="text-align: center;">For International Bureau use only</div> <div style="border: 1px solid black; padding: 5px; margin-top: 10px;"><input type="checkbox"/> This sheet was received by the International Bureau on:</div> <div style="border: 1px solid black; padding: 5px; margin-top: 10px;">Authorized officer</div>
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***What Is Claimed Is:***

1. An isolated nucleic acid molecule comprising a polynucleotide having a nucleotide sequence at least 95% identical to a sequence selected from the group consisting of:

(a) a polynucleotide fragment of SEQ ID NO:X or a polynucleotide fragment of the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X;

(b) a polynucleotide encoding a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X;

(c) a polynucleotide encoding a polypeptide domain of SEQ ID NO:Y or a polypeptide domain encoded by the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X;

(d) a polynucleotide encoding a polypeptide epitope of SEQ ID NO:Y or a polypeptide epitope encoded by the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X;

(e) a polynucleotide encoding a polypeptide of SEQ ID NO:Y or the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X, having biological activity;

(f) a polynucleotide which is a variant of SEQ ID NO:X;

(g) a polynucleotide which is an allelic variant of SEQ ID NO:X;

(h) a polynucleotide which encodes a species homologue of the SEQ ID NO:Y;

(i) a polynucleotide capable of hybridizing under stringent conditions to any one of the polynucleotides specified in (a)-(h), wherein said polynucleotide does not hybridize under stringent conditions to a nucleic acid molecule having a nucleotide sequence of only A residues or of only T residues.

2. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises a nucleotide sequence encoding a secreted protein.

3. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises a nucleotide sequence encoding the sequence identified as SEQ ID NO:Y or the polypeptide encoded by the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X.

4. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises the entire nucleotide sequence of SEQ ID NO:X or the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X.
5. The isolated nucleic acid molecule of claim 2, wherein the nucleotide sequence comprises sequential nucleotide deletions from either the C-terminus or the N-terminus.
6. The isolated nucleic acid molecule of claim 3, wherein the nucleotide sequence comprises sequential nucleotide deletions from either the C-terminus or the N-terminus.
7. A recombinant vector comprising the isolated nucleic acid molecule of claim 1.
8. A method of making a recombinant host cell comprising the isolated nucleic acid molecule of claim 1.
9. A recombinant host cell produced by the method of claim 8.
10. The recombinant host cell of claim 9 comprising vector sequences.
11. An isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence selected from the group consisting of:
  - (a) a polypeptide fragment of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z;
  - (b) a polypeptide fragment of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z, having biological activity;
  - (c) a polypeptide domain of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z;
  - (d) a polypeptide epitope of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z;
  - (e) a secreted form of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z;
  - (f) a full length protein of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z;

- (g) a variant of SEQ ID NO:Y;
- (h) an allelic variant of SEQ ID NO:Y; or
- (i) a species homologue of the SEQ ID NO:Y.

12. The isolated polypeptide of claim 11, wherein the secreted form or the full length protein comprises sequential amino acid deletions from either the C-terminus or the N-terminus.

13. An isolated antibody that binds specifically to the isolated polypeptide of claim 11.

14. A recombinant host cell that expresses the isolated polypeptide of claim 11.

15. A method of making an isolated polypeptide comprising:  
(a) culturing the recombinant host cell of claim 14 under conditions such that said polypeptide is expressed; and  
(b) recovering said polypeptide.

16. The polypeptide produced by claim 15.

17. A method for preventing, treating, or ameliorating a medical condition, comprising administering to a mammalian subject a therapeutically effective amount of the polypeptide of claim 11 or the polynucleotide of claim 1.

18. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:  
(a) determining the presence or absence of a mutation in the polynucleotide of claim 1; and  
(b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or absence of said mutation.

19. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:  
(a) determining the presence or amount of expression of the polypeptide of claim 11 in a biological sample; and  
(b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or amount of expression of the polypeptide.

20. A method for identifying a binding partner to the polypeptide of claim 11 comprising:
- (a) contacting the polypeptide of claim 11 with a binding partner; and
  - (b) determining whether the binding partner effects an activity of the polypeptide.
21. The gene corresponding to the cDNA sequence of SEQ ID NO:Y.
22. A method of identifying an activity in a biological assay, wherein the method comprises:
- (a) expressing SEQ ID NO:X in a cell;
  - (b) isolating the supernatant;
  - (c) detecting an activity in a biological assay; and
  - (d) identifying the protein in the supernatant having the activity.
23. The product produced by the method of claim 22.



<110> Human Genome Sciences, Inc.

<120> 123 Human Secreted Proteins

<130> PZ010PCT

<140> Unassigned

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&lt;221&gt; misc feature

&lt;222&gt; (369)

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&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (386)

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&lt;221&gt; misc feature

&lt;222&gt; (408)

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&lt;221&gt; misc feature

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&lt;221&gt; misc feature

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&lt;220&gt;

&lt;221&gt; misc feature

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&lt;221&gt; misc feature

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&lt;221&gt; misc feature

&lt;222&gt; (739)

&lt;223&gt; n equals a,t,g, or c

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&lt;211&gt; 1447

&lt;212&gt; DNA

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&lt;220&gt;

&lt;221&gt; misc feature

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&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1432)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

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&lt;223&gt; n equals a,t,g, or c

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<210> 18  
 <211> 1422  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (1397)  
 <223> n equals a,t,g, or c

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<210> 19  
 <211> 1107  
 <212> DNA  
 <213> Homo sapiens

<400> 19  
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&lt;210&gt; 20

&lt;211&gt; 1183

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (266)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (426)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1170)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1178)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 20

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&lt;210&gt; 21

&lt;211&gt; 1420

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

<222> (524)  
 <223> n equals a,t,g, or c

<220>  
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 <222> (585)  
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<220>  
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 <222> (596)  
 <223> n equals a,t,g, or c

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 <223> n equals a,t,g, or c

<220>  
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 <222> (1350)  
 <223> n equals a,t,g, or c

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&lt;210&gt; 22

&lt;211&gt; 1575

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 22

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&lt;210&gt; 23

&lt;211&gt; 541

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 23

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541

&lt;210&gt; 24

&lt;211&gt; 833

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 24

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&lt;210&gt; 25

&lt;211&gt; 1555

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1248)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1389)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1391)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1393)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1396)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1551)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 25

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aagcagtgga	aagattgaag	tcaaacagtc	gggcccatgt	gtgtgtctta	cttcaacctt	1380
tggtgtgtna	nangngcag	tttgtagagg	agacctctta	caaatgtgac	tttattcaaa	1440
aaattacaaa	aacattgccc	gatgctaaca	ctgactttta	ttatgaatgt	aaacaagaaa	1500
gaataaaaag	atatgaaatg	ttaaaaaaa	aaaaaaaaa	aaaaaaaaa	naaaa	1555

&lt;210&gt; 26

&lt;211&gt; 1543

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (69)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (717)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (899)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 26

gagcgggata	acaatttcac	acagggaaca	agctatgacc	atggattacg	ccaagcttgg	60
aattaacntt	cactaaaggg	aacaaaagct	gggagctccc	accgcggtgg	cggccgttct	120
agaactagtg	gatcccccg	gctgcaggaa	ttcggcacga	gccgaacagt	aggacatgtc	180
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aagactgggt	aatttataaa	ggaaagaggt	ttagttgact	cacagtcttg	catagctgag	360
gagacctcag	gaaccttata	atcatggcaa	aaggcaaaag	agaagcagac	aggacagagt	420
gaatgccagc	aggagaaatg	ccagacgctt	ataaaacat	caaactcttg	gagaactctt	480
cactatcata	agaacggcat	ggggaaaact	gccccatga	ttcagttacc	tccacctggt	540
cccacccttg	acatgtggga	attattacaa	ttcaagggtga	gatttgggtg	gggacacaca	600

gccaaatcat atcaccatcc cttgaaccaa aacgaacaag gctgacctta tttgcaacat	660
tctaacttgt ctaaaggctg cctgaagaat tgatccctga ttcacctaac tcagatntct	720
gctaggagac aagcatggcc ttaatctcag atgaggagaa gcagtagtca tggctcagaa	780
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gacctcaag accccacaaa gatctcttgg gaaatttaag acaattaaaa gcagccatnt	900
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tggaaatgaa aaatataatg ggcacactgg ggatagtcaa acttaaaaat tcactagagg	1440
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<210> 27

<211> 1262

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (621)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (641)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (722)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (723)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (726)

<223> n equals a,t,g, or c

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<221> misc feature

<222> (730)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1259)

<223> n equals a,t,g, or c

<220>

<221> misc feature



&lt;222&gt; (1261)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 27

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tgttttatta	cttactttta	tagcacttag	tcccagtggt	attagactgc	tatttggttt		120
catacaaaaa	ggattaaatt	taaattcatt	catgtttaga	cttgagttat	tacattttta		180
aaactatcat	cttgccttta	atgtttgtgg	tcctacacaa	actattagta	catttcagta		240
tcctcttacc	cctttgtttt	taagtttttg	attgctaaag	caagactttt	ttcttctaga		300
atttaagtca	accaagtgtt	atctatgttg	taaaaatgga	taatagtaga	ttttaggtga		360
taaaacaact	tgtagtaga	acatttctta	gcttaaaaaa	aaaaatcaa	aattccatga		420
tagaaatgca	gacctgtgag	ggaaactcct	gaaaagcata	agaagcatcc	cagagagcca		480
tgggtttttt	agaccagaga	atttagaggg	agattgtgga	actgaggcct	aggtgggtcag		540
atcgtttccc	ttatcactgt	aatattttct	gggggaaaaa	tgctttctga	gttggttaaa		600
caagcatcct	tacatttttt	ntttaattaa	aacagcctgt	ntagggcttg	ggattcccta		660
atactacagt	agcagtatat	gaatatgatt	ttgtgattgt	gttttttaaa	agataagtaa		720
tnngangan	tggtcttttg	cagtcagaaa	acactcacia	aaagacaaaa	aaagttccac		780
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catagcattc	ttaccttttt	ttcctattct	aagaattaaa	aaaaaaaatt	atagagccag		1140
caagggagga	ggcaggaaac	agaaatcgaa	tttcatcatt	ccagtatagt	tgcccttttt		1200
tttgattttc	tgacttggtt	ttataattat	atttacttac	taaaaaaaa	aaaaagggna		1260
na							1262

&lt;210&gt; 28

&lt;211&gt; 753

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 28

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ttgcttcaca	tagttttctc	ccctcaagga	gtctagccca	gactcccat	atgtcagtct	120
cagggtagca	tttcaagagg	gataaggtag	acgtttctgg	cctgtgtggt	tgtaggctgt	180
gaattacat	aacatcactt	ctttgagatt	ttcttggtca	aggcaaatca	catgacaagg	240
actcaagagg	gtagagaaat	aggttctact	atttagtgga	aaggacagca	aagtgcacac	300
acaaagagga	atgcatatag	agatgggggg	aatatgtgac	caactttagt	aatcactgta	360
attctgaatt	gactcacaaa	cactatcaag	acggatcatt	gtcataccct	agttcaaaaa	420
gcagtccttg	cagcaatata	gaacagatag	aagtgaagag	aatgtgattt	tgctaaaaat	480
gacatattta	catgaccagt	gatgggtgag	acctatgaaa	aatccccaga	gattctcaag	540
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cacctagtat	attcctaggt	atgtgtatct	aagcccaagt	tgggtctcacg	tttttgctta	660
cttccgagtc	aatatgtgac	atgccatccc	acctttttgt	gttaccacat	tattataaca	720
taaggggtgg	ttatgtttcc	tggatatctt	gag			753

&lt;210&gt; 29

&lt;211&gt; 1621

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (527)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

<221> misc feature  
 <222> (542)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (553)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (701)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (731)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (906)  
 <223> n equals a,t,g, or c

<400> 29  
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 ttttaaaaaa ccatggcaga tgtggacca gatacattgc tggaatggct acagatggga 180  
 casggragat saaaaggaca tgcaactaat accccttgaa cagctatgca tgrtgctttt 240  
 gatgtctgac aacgtggatc gttgttttga aacatgtcct cctcgcactt tcttaccagc 300  
 cctttgcaaa atttttcttg atgaaagtgc tccagacaat gtattagagg tgacagcccg 360  
 tgccataaca tactacctgg atgtatctgc ggaatgtacc cgaaggattg ttggggtaga 420  
 tggagctata aaagcacttt gtaatcsttt ggtagtagtt gaacttaaca acaggactag 480  
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 ancagtcttt gangctggtg gtttgaatcg tgttgcttac cttccaagcg tgaacagtgg 600  
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 agatagttct ggggagcgt caccatcgga gcttatagat tgtattcgaa gtaaagatac 1260  
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 gagagatgaa gatgggaaaa ctccattaga taaagctcga gaaaggggcc atagtgaagt 1560  
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 g 1621

<210> 30  
 <211> 921  
 <212> DNA  
 <213> Homo sapiens

&lt;400&gt; 30

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atattgccct catgacactt atccttatgt atggatttct tcaatgctac tattgtgcct	180
tacatgtgcc ttgtattata gcatttttat agcatttctc acccaattgt ggctatttgt	240
ttacatgtct gtctccttgg tggaaactgt aactctgtca taacagatgc cattttatgt	300
cagtttagact tctttgggtg ccagtaagag aagctgactc taatctaaac caaaaggaat	360
tcattggacg gatgtgggtt ggctcacaaa atcaaaggga caactgcgga ccgatcttgg	420
aatgatgtct tgacaccaga acagctctgt gaattcagat aggggtagtg aattgaccat	480
ttcatcaaat gctgcagcaa gctaggttgt tccccaaag gaaattgagg agtgttacia	540
gaagaccatt aggggaacgg ttatctgggt gctgataata acaaatttcc atggcagtct	600
ctttgctctc ttgttgaaga ggtactccac catgggcctt gagcatctct acacatcctt	660
gctaagcgtg tcaaatttca agtcctaact gtctctgtct tctggaggag gagacaggtt	720
tggttactgt ttgttgaata aattactgag cccttcacca tgggtgcctc agctgtatgc	780
aaagccccct gtattgctgg gggacagagc aactggtact gccatgctgg tgctctggct	840
gtttgctgtt ggcaataaac tattctgttt tgggtcaaaa aaaaaaaaaa aaaaaaaaaa	900
aaaaaaaaaa aaaaaaaaaa a	921

&lt;210&gt; 31

&lt;211&gt; 2095

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (14)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 31

cccacgcggt ccgnatcgtc ctccctcac ttcagagggt ggccagagct gaatacccag	60
agagggacaa gtaagggtcc agttccaaaa catcatgagg atgtatcatc ccacgtgtct	120
cacctgacag ttacagagga aacccgcacc cagaatgcac gtgctgtctt atgggaacac	180
tcagcgcaga gtgtcaggt ccggccacac tcgggctgtg cttggtcgtg ccatggaatt	240
cctcaggact ttctcagcct ccctaattggc agaagccctt ttacagcaag acatttaccg	300
tttgtctgaa aatagccgaa ctgagccttt tcttcaggct atatgagaag tctctagaca	360
gtgggcaccg tcagaaagcc cagagccttg tgatagctcc caccctgcct ggctcagatc	420
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gacacttctc aggagagccc tgtcaagtca tctcccgctc gcattgtcaga gtcccgacg	660
ccgtgttcag ggtcaagttt tgaagagact gaagcccttg tgaacactgc tgcgaaaaac	720
cagcatcctg tcccacgagg actggcccct aaccaagagt cactcttga ggtgccagag	780
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aaagaaatag aagaactcac caagatttgt gacgaactga ttgccaaaat ggggaaaagc	1560
taactctgaa ccgaatgttt tggacttaac tgttgcgtgc aatatgaccg tcggcacact	1620
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 tagggactct tgccttaagg agtgtaaaact tgatctgcat ttgctgattt gtttttaaaa 1980  
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 tcttggaaw aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aattc 2095

<210> 32  
 <211> 1838  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (1076)  
 <223> n equals a,t,g, or c

<400> 32  
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 gatccacctg cctcgccctc ccaaagtgtt gggattacag gtgtgagcca ccatgcctgg 180  
 ggcaaaagat attttcaaaa cattgtmaat aacttctccc ccaaaccag acagggtctc 240  
 attctgttgc ccaggctgga gtggcagggg caccatcgta gctcactgca gccttgaaca 300  
 ccggggctca agcaatcctc ccgcctcagc ctgccaaaagt gctgggatta cacacgtaag 360  
 ccagtgcact cagtcttaag taacttttta aataccaaag gtagaaaagg aagaagaggg 420  
 aaaaaaaaaa taagcccata tatggaaaag gaaaagacag cagataaata taggcaata 480  
 gaggtggaaa atataatcac gtagaattta gtatagtaaa ggattatctc tgaanaacaa 540  
 aaacagaaaa ctatcagagc caataaaga aaaatggaaa tgactgggga aaaccactca 600  
 ctaatgagtt gaattgtcaa gagaaactga gaaagagtac tgcttatata aaaattatgt 660  
 gaaattaac aaataatgtat ttttagtaag aatgggtgtt aagcacttat ggaatataaa 720  
 attatcacct gttaataaag aatgcatagt aaatggatg gacaaagaat atgagtgaaca 780  
 gataaaatca gtttttaaaa aattttatta aagttgatta agcctattag tgaaagaaaag 840  
 caggccaggc acaatggctt gctcctgtaa tgccaatact ctgggagggtc aaggcaggaa 900  
 gatcacctga gccaggaggt ttgagataag cctgggtaac acagtgaagc tccatctcta 960  
 aaaaaattaa aaagtaaaaa aaaattagct ggtcatggtg acacacacct gtskccyas 1020  
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 aaaaccagta aaaagtgtgt taataagaat gtacacattt cccctactaa aatttattgc 1680  
 ttgtagtgtt aaaaaaaat cataaagttt tctcaaagcc aagcaaaaaa attatttggg 1740  
 acaagtagc aaactcgctg cattagaaga aaaggccatt tcttcacata tttgaatata 1800  
 ggcaccaaca catagttcca catgaaatta tatttcgg 1838

<210> 33  
 <211> 782  
 <212> DNA  
 <213> Homo sapiens

<400> 33  
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 ctgtaacttc aagcaagcta caagaatcta tactagggtt cagacctttg aggctgacag 180

cgagctttga gtttgatgac agtacctaaa atatattaag tgtactcagg aactggccaa	240
gcatgggggtg gggcttgta ggaactggt atttctttct tctatttga gtgaataaga	300
tgctcaatag acgactttta ctctctgtca atggctcgcat aactgtctct ttttagacac	360
ttatgaaatt gtctgaactt cctctctac ttctccaact ccagaagag tgaaggtaac	420
aaatgttatg tccaaaccac ggtttgttcc cagaccctgg ttccaatgc ccacctcttt	480
tccaagaagt ccaaagagac gccctcatc gcaaaggaag tgtaccgtg ctgcctcgat	540
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ccctcatcct cgttccccgc ctaccctctc ttcaacttca ttcattcatc caacattcgc	660
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acgttccctc ccgctaagcg gcttggcaga gtaagaggca tcccaaaact cgtgccgaat	780
tc	782

&lt;210&gt; 34

&lt;211&gt; 1560

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (461)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (497)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (499)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (595)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (621)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (622)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 34

ggctttttct gacattggtg aaccccctag actacaatta atccctttgc tacagacacc	60
tgtagccctt gctgcctcct ttttgtaag aggtcttata attttatgtt tgatgtccat	120
cttccccact tgattgaaat gcactattta tggaggagct atgtctgtat tgtttgttgc	180
tgatcccta ttgtctagca tagtgctga catacagtag aggtcaaga catatttgca	240
cattgattta tggaaaactg atactcaggt tctgaagaat aaataaatgc acctgaactg	300
tcaaagtgtc aaaagcaggc aatccagaaa tgtctggagg taggaatcac agctgcaaga	360
ggcacttcct ggtaacctc gccctccgac ctctagtgtg agccaccctt ttggatccta	420
cttcagcctt tctggagta gtggctcaca ggtttcctga nacaaagaga agaggcttga	480
gactattatt acatatnant cttctttaga agcaaagtgt gttcgtggat tgaattttca	540
accttacagt accaattata aatcctgagg cattctatca gttaagacaa cttanaatat	600
ttgatcccat tcagaacttt nncatttgtt ttaaagcagg aaaagtaaar gmagtcaatg	660

twmtaacyct tcttctttaa aatgtggatc atagtccctct tggggatggt tgttcattta	720
atattaacat tttttaagct tgscatgtwt cgtgggtgta tctgtttggt ttcccttgggt	780
aactgcattt tgccatgacc cttgatacca gctctactgc tacagcccta ggctaggcca	840
ccgtcatctg tggcctggac cctttcagtc ctaactgggt gccgtgtctc ctttcttagg	900
cccccaaca gttcatcttc catatccaca cacagtagcc cttaatgatg tttttaaagg	960
aatgagctat attagatga tttctttgcc caaaaactcc ttcaatgggt ttccacttac	1020
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tctgagtctg aacacaaagg tcaactgact aaagaggctt tttcccacca tccagtggaa	1320
atcagcacc cctctgtaac tgtgtaccac attgtcttat tctttctcat aggtctgaaa	1380
ttgtcgtatt catttttaat gtattttttg cctttttgtc cctgctaaca tataagcttt	1440
ttgaggtcag agactttctt ttcaactgtg tattcccagt tcctaaaaca gggccctaca	1500
catattggat gtttaataaa cattttattga ctaatacaaa tgaaaaaaaa aaaaaaaaaa	1560

<210> 35  
 <211> 1092  
 <212> DNA  
 <213> Homo sapiens

<400> 35	
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gccttatgat tctccaaagg acatttcccc cacgggctct gaggacatct ccgtggcttt	120
ccaaccccat ggggggttaa gggaaaaaaaa aaaaagggaac gtttatggaa atgatgctag	180
ggttgttctc tctcttttgc cttgtcactg gaattgctga aggcagggtc gaagatgctt	240
ctctacatga catctgcacc acccaacaca cacttacctt cacaccttca taccctgttg	300
gagggtcctg atgactacag ggcagtaaat tcagccccac agggaggcca cagcagcccc	360
cagcctctag cctcctaccc tcttctctag gcaaccttga caggaaattt tccctctgcc	420
ttctccttga tcccaacggt agctgcataa tagctgagct cacataatcc ctgtcgccag	480
tgctagagtg cccttagatg gaggtagccc aggtttgact tctgaaatcc ccagcagcag	540
gccttttctt tctagagctc ttgtcaggaa gagaaagctt tggaccagct catgctgggt	600
gtaatccttt gtggaagcct ccctgtttcc cttctctgat ctgccccgga gattcctgtg	660
tgctccagtc tctagggagg gaggcttagc tggagagggt caagggcagg agaaagcagg	720
agaatgcaga ggcgcggggg agaggacaga aagtatatca ttataacta acctttagcc	780
tttagccact caaaaatatt tcttaatagc ctaagggttc ttggcaggtc tttcccaca	840
tcagcaagaa atcttgggag ttgggaagag tcagaccttg ttccctgaac aagctttctg	900
ctttggccaa gagttgttag gagattaatg cctgtccctg aaaggcacag gttggagtgt	960
ttacttcttc ctctccttcc ctctctcccc ccttagagat cgtgaccctt cctgcttgcc	1020
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aaaaaaactc ga	1092

<210> 36  
 <211> 1153  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (409)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (511)  
 <223> n equals a,t,g, or c

<220>

<221> misc feature  
 <222> (1001)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (1089)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (1113)  
 <223> n equals a,t,g, or c

<400> 36  
 agactatcct caaggagctt acatatcagt aaataaatta ttaaagggtg aaaatgtggt 60  
 aaaagagaca taatgtctcg gagagagaac aaatttctgc tttaggagtg ttcttagtta 120  
 aggtaacatt agcttctata atacgcacac tcccaaatct cagtatttca acatgagttt 180  
 ctctcttgct catgtaaaga ctggtcaggg acccaggttg acagaggctc ttcagtacat 240  
 agcttccaag attgctgtgg gtgtgacatc cagccagaaa tctggtgaag agagagcaat 300  
 grttacacag gaacttttaa tggaccaggc ctgggacagc gtatgtcact tccaccaaca 360  
 tcccactcac cagaatttsg tcacagggcc atagctatct gcagagaang ctgggaaatg 420  
 gaacttagct atgtgtcaa gaggaaaagt aaaacagtta ttgaataatt agtaataatt 480  
 agcaagtaac tacctagggg tcacagagga nctctcaggt agaattttaga cttaaagatg 540  
 atgggggagt gtgtggaaga gtggtgcaga atagggaaag gggggattga aggaagaaca 600  
 agctctagct tcacctgcat gggtagagcc cacagtgttg gtagggacat gttagctttc 660  
 aacatcagct tcttaacagt attattcttt catcggagga aattagtcta tttctgagga 720  
 aaaaaaaatc tgcaatacgt agcaatttac ttacttggtat attgaatgtt aaagcagaga 780  
 gagactttgt cctcaaaacc ctcccatttc agaagtgagg agcctgggga ggtcatgctc 840  
 tctggatgtc acacagttag tcaactgtcaa agccagaata gaaccagac ctctcagttt 900  
 cccatwccag tgctctttct atgaggaaag tataagtttg agcattttta aaccttaatt 960  
 atgtagaat aacctatgata ttttatcgta aattatttca ntcattctcat tttaaatttt 1020  
 actccaaact aaaggaaaac ggtactgatt taaaacatct atcataattc aatatagccc 1080  
 atatttctnc tttaggaaaa attttttttt gtnttttatc ctgaagaccc gtgccctctt 1140  
 cctgtgtctc atg 1153

<210> 37  
 <211> 985  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (633)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (642)  
 <223> n equals a,t,g, or c

<400> 37  
 ggcacgagca caccctctg agaccaggga gcatttatcc aaggaaacac ttgtcttttag 60  
 aggatgttga cgatgcccc aacttactgt agctgtcagg aaaattaggt gagctattta 120  
 gtatcattga gttcatttt acagaaccag catgtgtgcc ttagacttcc ctctgaccc 180  
 tttagggtctc aacttacata ttgccctctt gagccttcta gttcccagac tgagttagga 240  
 accccaaccc atgctggact cagttagtcc tttccacatt gtgctgtaat tggctatacc 300  
 ccactgtgcc ttctgcccag actaggagtc tcctgcgggc cctaactgtc ccaatttccg 360  
 gtgtttggac tgggtgctctg tagatgttta gggaatgaaa gggtaatgaa taaattaatg 420

aaacaaataa	gaatcatata	gtattagcag	cactagataa	aagggtgtaa	atcttaagtg	480
atccaccatc	ttttaataa	ttcattcaaa	cgatatttca	aatgcatatc	acctccaaga	540
aatcgtttct	gcatttcrrs	tgasttctac	gatgccwwrt	gaatgarraa	rsrrgracak	600
ggyrtggttc	tggggggctg	tgagagtaac	ggngcaatcc	tngtcattgt	cgtagttatc	660
tggccatcca	gggcttctca	ggttgccaaa	tgccttgtag	tagtctctgt	tgcaatctta	720
gaggaataat	aggcataatt	aatgtacgca	ttccaatatt	tagtgctctt	tcaacttaca	780
caggaatcat	tcaaaaagat	cattgcattt	gataaacttt	agaaaaaagt	aatccagctt	840
cttcgtttac	ctttgagata	attgagaccc	tgagcagtga	agtgaattgc	tcaagcagca	900
cacacaggtg	caacgcaaca	gctcgttcac	acaaacacgc	ctacaggaag	catgacacag	960
gaggcttctc	ctttaagac	gaata				985

&lt;210&gt; 38

&lt;211&gt; 1122

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (380)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (381)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (402)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (499)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (505)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 38

agtgaagc	agatgttaag	tggcatatgt	gtcttcagtc	acctctgtgt	gggttgttct	60
gtagtataga	gggtgttcta	aaaatgatct	ttaggaatgg	agtgaggctt	gtttttgttt	120
ttgttttgtt	ttacacttcc	acacaatccc	ttttcaattc	cttgcaaact	gctgagtatg	180
tactattttg	ccagcaaaagg	ctgagcctgt	atgaaccag	ccatgtgctt	tgtctgtgca	240
tgccccaca	caggaagcac	accagagaaa	gcgatacttc	agggtagatt	gatttcatta	300
ggaacttcat	tatcaccagc	ctcaaatggt	tctggccagc	agtctttttc	tatctgtatg	360
attaaccctt	ctctgcgcgn	nagcacctcc	tcccaccacc	tnttctcagt	gttaacagggt	420
gatctagact	cctactctca	gagaaaattg	aagccaacaa	gtagaaagtc	ttttttgcta	480
ccaaagacac	aaacctatnt	tgtnntgcat	ccatccctcac	ccccgctggt	gcttgttcaa	540
cacaggagtc	ctctctccac	ctacccaaag	cctgtcccct	cctgctgtgc	cctggatctt	600
atctctgtga	ttgccttaga	aacctttctt	gtatatattc	atctttttcc	ttcaatagat	660
ctttcttatt	ggattttaag	catgttgcag	cctcttctgt	taataaaaca	acaatcaaca	720
aaaacactct	cccttaactg	catgctttat	tccagctact	accttatatc	attcctttcc	780
ttcaaggcca	aagtcctcag	aagagggtgc	aatatcctcc	atcatttctt	catttcatac	840
tcattcttca	acacatacta	atctagtctc	ttaccccata	attcattaaa	acacttatcc	900
ttgggtcatg	ggtgacttct	gtatagctaa	atccagtgga	tatttttcag	gcctcctctt	960
ccttacatct	tagtatttca	ccctattggc	cattcttttc	ttcttgaaat	actctctcct	1020



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ttccctctgt aaacttgccc tctttcacia ggccagtaaa ca 1122

<210> 39

<211> 598

<212> DNA

<213> Homo sapiens

<400> 39

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gggtctcagc gcttaccact ggtcctggcg tcacggactg tggagctggg ggcagcccg 180  
ggtgggtttt atagcaagtg gtgagatgtg ggcgctgtgc tccaaaccag accccgttaa 240  
gtgccacatg gtcaacagtt tagtgtgcag aaatgaattt ccttctctta attttccctt 300  
atttttccag cctgttgggg gaggtggagg tggtgaaatg ttagcagtga ccagttcatc 360  
ctgatctgct tgggaccttc cagtttttagc actgaaagcc ccacagccca agaatccctt 420  
ggatatcaac cacggttccct ccttcagaa tgtcccaaga gccttagggc ctggagacac 480  
acaggtgggg gcctgagccc ctgtccccct cctccagatg gagcaggcag ggccccaggg 540  
ccccagggct cacggtgttc tggggtccac agtgtgctgt gcggccaggc tggctctc 598

<210> 40

<211> 1129

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1053)

<223> n equals a,t,g, or c

<400> 40

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aaatatattag tcagttctgt tttgccaca attagcatgg ctaggtcatt gatttcagca 120  
ctcaggtcag gtatgtcccc aggaaggggtc tcagtggttt ctttgcaggg atcacagcta 180  
tgtcttttgg tatctattgc aatcatgggt ttgcttctat tttgaatttg tctgtcttat 240  
ctcttgagca tcaaaagtgc ccttcagggt aggcattgcta cttgttttat atctgccacc 300  
caatttcaac tgtaaaatcc taatcacaag tggcaactag atagggttaa atgatttctg 360  
gaactttcct tctggacatg taagatccta aaatcttacg agaatttcag tgagttgatt 420  
ttgtctttaa tattttttct taggaaaaag aagaccatt ttgaatctgt tcaactgaaa 480  
acctcaagat ccccaaatat atgaagagac agtgctgtag cccttgagac taatgaacaa 540  
agaaacctgc tctagtttta caggaccata ttttaggggtc tgcctcata cctgtcacat 600  
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tgccttatca catgggtcaag taccttgcca aataaaggaa agcaaatgat ttgggtctca 720  
actgaagatg aagctcaact caggaagaga tttatctgta tatacacata actgaaaacc 780  
aagtttaagc ccaccaatgc actgctgatg catgccatat aattaatggg taactttgat 840  
tctttatgac gtctacataa caagtgtgat ttggaaggca catgtgagca tatgcattat 900  
gatccaattt atgttttttc tttgtttata ttttggggaa aattaaaatt tttttaaggt 960  
atatttttcc cattatttat tttcctgacc ttaaaacagc ttttctacta aaaaatgggtg 1020  
agcaatgaag acaataaatt tttcattttt ccnaaaaaaa aaaaaaaaaa aaaaaaaaaa 1080  
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaacc 1129

<210> 41

<211> 1158

<212> DNA

<213> Homo sapiens

<400> 41

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caatagggt	gaatgaattt	accaaaggaa	gctgccttat	attatatgcc	aggctgctgg	180
ggaaagcctc	aggtcctggc	cagccctgt	tctcacaaga	acatgcaggt	taccacataa	240
ataatggcat	atgccttcca	taggacgtca	acctgactta	aatctaccta	taccctactc	300
tctattcttt	ggtttttggt	tctcatccct	gtggaaggaa	atgggcctct	tctggcatct	360
catgctactc	tgtgcttttc	cttgggctcc	aaattctagc	tcataaagat	gcaagttttg	420
caatttccct	ttaaagggtta	agaaaagagc	aagctgtcca	gagagtgaga	agtttgaaaa	480
gagaggtgca	taagagagaa	atgatgtcca	tttgagcccc	accacggagg	ttatgtggtc	540
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ttgattggct	ttacacaact	ggcatttagt	ctgcattaca	caaataagaca	ctaatttatt	660
tggacaacgc	agcaaaatga	gaactttatt	tggtgcagtc	agggctccat	ttagttccct	720
cactctgctt	ctaatacccc	cttctcccag	ccctcttcta	tttgatagag	gtctgtccct	780
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cttctaactt	ttaataaaca	tttaggtata	atacattaca	gtaagtgcta	tttagatata	900
aacttaaaac	atactatata	ttttaaggat	ctaagaatcc	tttagagaag	gcacatgact	960
gaagtacctc	agctgcgcag	cctgtagcca	gtttttttaa	tgtaaaagta	agaatgccag	1020
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aaaaaaaaaa	aaaaaaaaaa					1158

&lt;210&gt; 42

&lt;211&gt; 1767

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (765)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1130)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1545)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1658)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1744)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1748)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 42

ccgggtcgac	ccacgcgtcc	gattgaacgg	tttggggcat	ccttcctagg	aaaagaatgt	60
cagttaaggt	gggtctctt	ctgggttttg	tgtattttac	cctgggccca	gttgttgacg	120

aactggaggt	gacctgcct	tctcattcct	aacatttttc	tctactacca	cccgattttt	180
gaggcagacc	cccaactcgt	catggctcca	gctgaagttt	gaaatataac	gtcccggact	240
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aggctgaaat	gcagactttc	ctcatcttcc	acagtaagca	ggattccctt	ctgataacct	420
tgtcagaaat	gttgtttttc	aaagggcatg	tatggtatct	gtcactttca	gtgatgattg	480
tgctgcagct	tgatgtctct	tgacctgaac	tgagtatgcc	tgtggaaggt	cctcttagcc	540
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aacagatact	taatttattt	caaaaataag	gaaaaataga	ggaatcgggt	tgaatgtttt	960
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ataatgtcaa	gactgaaagt	ataaaaaatg	tacatataag	attaattttt	atatcttttt	1140
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tgggatcatg	agttcaagcc	ccacgttagg	ggtagagttt	actttaaaaa	taataaaaag	1260
gggttgagtc	tattgcaact	agctctacat	gactaattta	aagtggagag	atgttggtgt	1320
agatttataa	aaaataacta	gttttcttaa	tgtgtctttg	tatgatcaac	agcatgccat	1380
aagcaataca	aaacaccgaag	ccttataact	acaagaaaaa	aggttaacat	actggtaaaag	1440
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ttgcataaatt	tggaaaaggt	tgctttgaat	gtaggacnaa	actgtttcaa	agatttttgt	1680
ttgaaaagtt	tatgtatttt	tgtgccttaa	tatttgttct	gacttttaat	aaaatgcttt	1740
ctgnaaanaa	aaaaaaaaaa	aaaaaaaaaa				1767

&lt;210&gt; 43

&lt;211&gt; 917

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 43

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aaggggaagtc	gccagcctcc	atcgacacgt	ggccagggtcg	acgcagtggt	ggtatgatcg	120
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aaaaaaaaaa	aaaaaa					917

&lt;210&gt; 44

&lt;211&gt; 1987

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1554)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 44

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ctgtgccag aatggatgac caggaacctt caagagtggc tgaaaagatt gcagagttat   1920
cataataaat tgctaacttg cgtatwaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa   1980
aaaaaa                                           1987

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&lt;210&gt; 45

&lt;211&gt; 2053

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 45

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2053

&lt;210&gt; 46

&lt;211&gt; 1272

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1264)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 46

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gtatgaagag aaaaatcagaa agctggaaga taaagtggag caggaagaaga gaaagaagca    180
aatggagaaa gaaactagca gaacaggagg ctactatgc tgtaaggcag caaagggcaa    240
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1272

&lt;210&gt; 47

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 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (459)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (503)  
 <223> n equals a,t,g, or c

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<210> 48  
 <211> 2119  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (1424)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (1438)  
 <223> n equals a,t,g, or c

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 ggtgtcggtg gtcgcagcct tggcgctggc ggtactggcc ccgggagcag gggagcagag 180  
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 atttgggaaa ctggactata cttcaggaca tcaactcatt agtaatcgtg tggaagcgtg 540  
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&lt;210&gt; 49

&lt;211&gt; 1188

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (577)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1022)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1052)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 49

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<212> DNA  
<213> Homo sapiens

<400> 50	
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ggtaagcaaa	ataaattgta
120	
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taaaggaact	ctttgcactg
ctataatgaa	cagcccccaa
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cggtgattca	gggaccagc
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tgccttttaa	aggtcctcag
ggtgctctcc	atgtatcttg
360	
ccaatgggga	acgagtgtgg
aggactcaca	agcgggtcyc
acatcacgtc	ctccggggct
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478	

<210> 51  
<211> 1333  
<212> DNA  
<213> Homo sapiens

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<223> n equals a,t,g, or c

<220>  
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<222> (486)  
<223> n equals a,t,g, or c

<220>  
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<222> (493)  
<223> n equals a,t,g, or c

<220>  
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<222> (496)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
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<223> n equals a,t,g, or c

<220>  
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<222> (633)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature



&lt;222&gt; (1330)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 51

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&lt;210&gt; 52

&lt;211&gt; 1255

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (541)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (542)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1156)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1162)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1223)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 52

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&lt;210&gt; 53

&lt;211&gt; 1140

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 53

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&lt;210&gt; 54

&lt;211&gt; 1220

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1197)

&lt;223&gt; n equals a,t,g, or c

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 <223> n equals a,t,g, or c

<220>  
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 <223> n equals a,t,g, or c

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 <212> DNA  
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 <222> (621)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (651)  
 <223> n equals a,t,g, or c

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<210> 56

<211> 988

<212> DNA

<213> Homo sapiens

<400> 56

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<211> 1500

<212> DNA

<213> Homo sapiens

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<222> (71)

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<220>

<221> misc feature

<222> (73)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (755)

<223> n equals a,t,g, or c

<400> 57

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&lt;210&gt; 58

&lt;211&gt; 1391

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 58

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&lt;210&gt; 59

&lt;211&gt; 1579

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 59

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<210> 60

<211> 1241

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (8)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (59)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (78)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (84)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (86)

<223> n equals a,t,g, or c

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<221> misc feature

<222> (104)

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&lt;221&gt; misc feature

&lt;222&gt; (128)

&lt;223&gt; n equals a,t,g, or c

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cactgatgta accaacctca cagactagtt gttattata ttaatagttt gagcatataa	900
agaggaactt gtgatgggag agatctaggg aggagtaaaag aagtatagga atgtctggcc	960
tgtattctct tcacctggga ccactgattt ttaagctgcc acattggctg gagaacaggc	1020
tatggagtcc ataattgtgtg gtctcctgga gctcctgttc agctctgcct tctttgaggg	1080
ggcagggatg gggcagggag cacatygtaa tactaacggc ctccagagmtg cccctgatg	1140
tcctcctgcc tgttaccctg tgcctctgtc tcttaacagt gggatgatga agatgccacc	1200
gtcaacaagr ktgcgtcga gctgtgcacm tttaacctgg g	1241

&lt;210&gt; 61

&lt;211&gt; 930

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 61

gaattcggca cgagctaagt cctgatatcc catgatgttt tttgttttac tttgtttttg	60
gctatttctt ttttctaaaa atagccctct ctggggaatg ctgagatctt cattctttat	120
tagtatcaat ttataattat ctacatctgt aagcagttat tcgaaagtct ccagatctta	180
ttctatcctg gcacccatgg tgactaaaaa aatcaaagac gttaaattct tgaagcagc	240
cttcaaacca cactaccata ccaacttacc ttatatgtcg gggagttagt gagcaaatac	300
attaattaac ttgacagaag ttgcacactt tctgtacttc tgaacaaaaa tttggatgca	360
tgtttttctt tatcatgagt cacacctgat taggatttcc ttagcttttg ttggggtcag	420
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catggatttt gtaatagtcc tggacattca tcagaaagta acctgtagt gggctgccta	540
cataggattc ttcctttgaa aagccttaaa catttttcta atggttggtc tctcttaact	600
aacaataaaa aacagcaaca atgcasctgg gcacagtggt ttttgctgt aatcccagca	660
ctttgggagg cccaggcagg tggatcaact gaggtcagga gtttaagacc agcctggcca	720
acatgtgaaa ccctgtctct acgaaaaata caaaaattag ccggatgttg ttttgacac	780
ccgtagtccc acctactggg gaggtgagg caggagaatt gcttaaaccc aggaggcaga	840
gcttgcatg agctgaaatc gtaccacagc actccagcct gggcaacaga gtgagactcc	900
atatccaaaa aaaaaaaaaa aaaaactcga	930

&lt;210&gt; 62

&lt;211&gt; 998

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 62

ggcagcaggc ttaagtcaag ccacctgatc agtcttgtaa ccactggaga gatgagcagt	60
gttttagtcat gtccctaata ctgttattgt cagtcaccct tttacatctg tcttttctg	120

ttggcttctt	tctttttagg	ttgtagggga	gacccattgt	ctagagagaa	tatacgcttt	180
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agatgtggag	gtgaagatat	aaagtaggtc	tcagctttgg	ctggccaata	tgggatccta	300
cttatctcct	caggggactg	gacaattcgt	gtcaagactc	tgtgcttcag	gagcctctgc	360
ttcttcctcc	ttcatgggtcc	aactttcctg	ccccttcttc	atctcattag	cttaaccctc	420
agttgcctga	cccaagtcaa	ggtgtgtgac	ctggtcctga	tcaccacctc	tttttggggg	480
cttctgcaac	tgtgctctgt	cctggcaacc	tgcttctgta	atctgtttat	ccccaattt	540
gaatgagtaa	taggaattgc	ctaaattttg	gataaattat	cctacaaaat	aaaagcattc	600
tcacattgcc	ctctcaaadc	acatgatctt	tgtagaaaaa	ggccggtccc	tatgaagcta	660
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gagatggagc	ttgcagttag	ccgggattgc	gccactgcac	tacagccagg	atgacagagt	960
gaggctccat	ctcaaaaaaa	aaaaaaaaaa	aaaaaaaaaa			998

&lt;210&gt; 63

&lt;211&gt; 1193

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1080)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1186)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 63

ggtcgaccca	cgcgtccgca	ccgaagccca	gagggctctg	gggcacaaga	ctgacgccag	60
ggtatgaaga	gtgtattttt	cattcaaagt	gttattttgt	ttttccttcc	aatgtctgga	120
gaccaccagg	gcattctctg	gctggatgag	ctcccacaag	cctgagggaa	aggccagcac	180
tcgctagcag	tggcaggcag	aggcccaggc	tgccgtcccc	tagagtccca	ggttggctct	240
gccagtgcct	gtcctttacc	aaagatgaat	gaagcaaatg	tcatgctgcc	ttattcaggg	300
aaggaggagc	ctgtcctcgc	tgtggccatg	accctgcctc	tcccaggcag	gggcccgcga	360
tgtggaactg	ctgccactga	gggggggatcc	agttttgtca	atgcagttgt	ctctgtttta	420
caagttggag	tactctttat	gctgtaccca	gtttctaaac	tggagactgt	gtgtgccctc	480
tggctctgag	taccctctgt	ttgggcttgg	gcctaggctg	cattgaaaag	agctgaaggt	540
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cgacacggts	ggggcatctg	gcctggccag	tgccctgata	ccagagagcc	cgaggaggtg	660
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aagcccatat	gtaccacca	gctgtgtcca	aaaccgccag	ctctgttctt	cctcagccag	780
cctcgcccat	ccccttgagg	tctcagcccc	tttcccttgt	agctcctccc	ctggaggggg	840
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tgttgacgat	gcacttttat	gaaatgtagt	ttctatcgct	gttttnagcc	ttt	1193

&lt;210&gt; 64

&lt;211&gt; 830

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens



&lt;400&gt; 64

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ggtcgaccca cgcgctccgct gaaaggaaaa gcactgtttg gagaatgac cacctttcaa      60
gattttactt attgttgata atgctccac atgtcctctt ttttacgggt gatcttcatt      120
cctaataatca aagtgatatt tcttcctcca ggcaccacct ctttgatcca cacaatggat      180
caaggagtta tagcagcttt taagttctac tacctgagaa gggaggactt ttgccagtc      240
ccatactgca gtggaggaag aactgagaa gactctgatg aaattctgaa cagcatcaag      300
aaccttgttt aggcttggat tatgtcgcta aggactgtag gaatggcacc tggaagaaga      360
cacgcaagag gtttgtcaat aayttcaaag gatttgccaa ggatgasgaa gttgcaaaaa      420
tcaagaargc tgtggttgag atggcaaaaca actttaacct ggggttggat gtggatgaca      480
ttgagtaatt cctagagggg gttcctgagg aattgactaa tgggttgctg ttggaactgg      540
aataggagtg catagctgaa gaagaggtaa agaaaaagaa agtgcaggag aagggaaaaa      600
agaactccca agaatactca cagtgatggg tttagcagaa gcttcttcag actccaacaa      660
gtcctctaag aagtctgaaa acatggaccc caaaactgaa aggttttcac taatagagag      720
gaaagttcat ggtgcattat ctgcctacaa gcaaaaccag gattcaaaaa accctttgag      780
ctggagcttc aaagcacaaa aaaaaaaaaa aaaaaaaaaa aaggcgccgc      830

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&lt;210&gt; 65

&lt;211&gt; 867

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (457)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 65

```

ggcgcgcctt tttttttttt tttttttttt tttttttttt gttaaagtgc tgatgccaga      60
tgacccttga gatcccttat tagtgaaatg ttctgataat aaagaagagt ttggctcacc      120
tgctggtctc caccacacag gtttataacc aagagcccta cagctcttgt cccaccctga      180
gggcctgact gacctgtgga gggcccccacc ttctgcctcc attcactcac cctgttccc      240
aagaaccact gacttcttta catgaagcct actttgagta agtttttagg tacagatgct      300
gaattacceca agctgtatcc accctcactc caggcacccc gaggagagac tcaactgctt      360
ggcccagggt tagagaggcc cacacgggaa ggcagagtgg agcagatggt atttaaccaa      420
aagtctgtat cctggggctc ccagctacca cagtcangaa acacattttt aaaaaatcma      480
gacccttgaa ctagcagcag tagtcaccca taccgtatac gataaataaa agtaagccaa      540
tgttttattct tctttgcata aaatcaccta taccaacact tatacattac agcatcattc      600
agttaattca agtctgaatc ccagaaactc tcctgaaatc aagccacagt tcagccctat      660
tcttcttagt ttttcttgac atacttttgc ttactctata aatccacgga tattcttctt      720
gcctactccc accaaagccc aaatacacgt gaaaaaagtt aatcatgaag tttttcttat      780
tcccttacat ttagaaaatc agcatctact ctcatagact acttgtaaga agacaaattt      840
ctgtactacc ggacgcgtgg gtcgacc      867

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&lt;210&gt; 66

&lt;211&gt; 685

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (7)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 66

```

ggggccnttt gggggccccc cctttttttt tttttttttt tttttttttt tttttttttt      60
ttttttttt ttggacagg aagtagaatt tattggtgag tattaagagg ggggcagcac      120
attggaagcc ctcatgagtg cagggccgc cacttgtcca gagggccacg actggggatg      180
tacttgaccc cacagccatc tgggatgagc cgcttttcag ccaccatgac ttcaaattca      240

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tcagcattga	acttggtgaa	gccccacttc	tttgagatgt	ggatcttctg	gcggccagga	300
aacttgaact	tggccctgcg	cagggcctca	atcacatgct	ccttgttctg	cagcttggtg	360
cggatggaca	tgataacttg	gccaatgtga	accctggcca	cagtggcctg	gggctttcca	420
aaggcacctc	gcatgcctgt	ttggagcctg	tcagccccag	cacaggacaa	catcttgttg	480
atgcggatga	cgtggaaggg	gtggagccgc	acccggatat	ggaagccatc	tttgccacaa	540
ctttttacca	tgtacttatt	ggcacaaaatt	cgggcagcct	ccagggcttc	agaggacagc	600
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ttccgcccc	ggttataaaa	gcgaa				685

<210> 67  
 <211> 801  
 <212> DNA  
 <213> Homo sapiens

<400> 67	
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gtggtactat	gtataagacc
tcctcactg	actatttggc
cacaggcact	gtgtgctcca
cacagcctca	gtttgctgtg
ccagctctct	ggctcctggaa
ccttctccaa	caaggcctga
tccttgggta	ctctccctca
gttattcttc	tatcactgtc
aaaaaaaaa	aaaaaactcg
	a

<210> 68  
 <211> 908  
 <212> DNA  
 <213> Homo sapiens

<400> 68	
gaattcggca	cgagatttta
tctaactatg	atactttcaa
ccttgttacc	tagaactctt
gaagaaat	ttactttggt
taataataaaa	ttttgacttt
tacctatctc	ttaaaaatat
caaaaactta	gaaggtaaac
ggtttcagat	atgcacagaa
gcagtcagtt	tctctgacct
taagtgtgat	acaccaactt
tgatgcatct	tacttagaaa
tatggatctt	taatacagaa
agccaggcca	gttggcatga
aggggtgtca	gtgtggcttc
actctttgtc	tttattacaa
aaactcga	

<210> 69  
 <211> 696  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (605)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (648)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (655)  
 <223> n equals a,t,g, or c

<400> 69  
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 ctactccaca aaataatttt ttctttttgc agttgaaaat taactgcatt attactaat 180  
 taataaaata aatcaagtgg tataagggat tagtttacc tcaagccgat gactccatgg 240  
 ctactgatat tagttagttt wggattttta aaaagcata cagaccccca gtttcaggaa 300  
 ttgagtataa atattgcttc ttgtcacctt gggacagtaa tgccttatag tggcactagt 360  
 caccttaagt agattacaca tgggtgaggt gaataaagct gcatgggaat ttgctttcgt 420  
 gatataattc atttgcaaac ttctacataa tcaagtttta tgtttaaaac catcggttct 480  
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 tccccagtc tcttattggc tatgttaaaa aaaaaaaaaa aaaaaagggs ggccgctcta 600  
 kaggntccaa gcttacgtac gcgtgcatgc gacgtcatag ctcttctnta agggncacct 660  
 aaattcaatt cactgggcgg ccgtttacaa cgtcgg 696

<210> 70  
 <211> 455  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (431)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (432)  
 <223> n equals a,t,g, or c

<400> 70  
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 cccggtgacc agccccgagt gactcacgga ccatgagcta gaagctgccc ttgcaggagg 180  
 cttgtcatgg gtcgggggtg ccactcagg atgcaggctc tccccagggg gccccaggct 240  
 cgctgactg aagacatgaa ggacctagcc taggagtggt cagggtccc ggagtggcca 300  
 ggggtcccgtg tgtkccctct gccagtcttc gctctgtccc cgttcaatca acccatctc 360  
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 aaaaaaactc nngggggggc ccggtaccca atttg 455

<210> 71  
 <211> 413  
 <212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (343)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (385)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (410)

<223> n equals a,t,g, or c

<400> 71

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gggtttccaa tcaggccgag tggtttgagg acgatgtcat acagcgcaag agggagctgt	180
ggccacctga gaagcttcaa gagatagagg aattcaaaga gaggttacgg aagcggcggg	240
aggagaagct ccttcgcgac gccacgcaga actcctgagg cctccaagtg ggagtcctag	300
ccccctccct gatgaaatat acatatactc agttccttgt tanaaaaaaa aaaaaaaaaa	360
aaaaaaaaaa aaaaaaaaaa aaaaanaaaaa aaaaaaaaaa aaaaaaaaaa aaa	413

<210> 72

<211> 849

<212> DNA

<213> Homo sapiens

<400> 72

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taagaggact ttaggttact gagtcacca tggatcatgt ttgcagagaa gtgtcacaga	180
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aaaaaaaaaa aattagctgg gcatgggtgt gcctgcctga aatcccagct actttgggag	720
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aaaactcga	849

<210> 73

<211> 505

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (12)

<223> n equals a,t,g, or c

<220>  
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<222> (501)  
<223> n equals a,t,g, or c

<400> 73  
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tatagtgttg atctgggtcc ccattcaaat ctcatgtcaa gttgcagtcc ctagtgttgg 180  
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catccccctt ggtactgtct ttggcatagt gagtttgttc tcctgagatc tcatttttta 300  
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ctcactcttt gtttgccttc taccataatt ggaagctttt tgaggcctct ctagaaacag 420  
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aaaaaaaaa aaaaactcga ngggg 505

<210> 74  
<211> 719  
<212> DNA  
<213> Homo sapiens

<400> 74  
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cggcctcaat ttactctaaa atgtgtaccc tcatagctac taagaaagt gttgcaaaaa 180  
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aca\*accatt ttcttttttt taaaaccctt ttttttkttt ttttttttga gacagaatct 360  
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tcgagaccat cctggctaatt gcggtgaaaa catgtctcta ctaaaaatac aaaaaattgg 540  
ctgggcttgg tgggtggcgc ctgtagtccc agctactcag gaggctgagg caggagaatg 600  
gcgtgagccc gggaggcgga gcttgcatgt agcagaaatt gcgccactgc actccagcct 660  
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<210> 75  
<211> 1274  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (1243)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1270)  
<223> n equals a,t,g, or c

<400> 75  
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tgctttatcc tgcatattat tcatacaaag ctgtgaaaac aaaaaacgtg aaggaatatg 180  
ttcgatggat gatgtactgg attgtttttg ctctctatac tgtgattgaa acagttagccg 240  
atcaaacagt tgcttggttt ccctgtact atgagctgaa gattgctttt gtcatatggc 300  
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aaaccatggt aaactttgga cggcaagggt taaaccttgc agckactgct gctgttactg	480
cagcagtaaa gagccaagga gcaataactg aacgtttaag aagcttcagt atgcatgatt	540
taacaactat ccaagggtgat gagcctgtgg gacaaagacc ataccaacct ctaccagaag	600
cmaaaaagaa aagtarccag cccccagtga atcagcmggt tatggaattc cactgraaga	660
cggrgatgwg raaacagatk aagaagcaga ggggccatat tcagataatg agatgttaac	720
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gtcatctaca cgtcaaatat cccaagacag attatgctaa atacatcgac ttcattctct	900
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aagtgcacatn acaa	1274

&lt;210&gt; 76

&lt;211&gt; 519

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (13)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (24)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (35)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (44)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 76

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tactagccag tgtggggaaa aggtacaata tgtcaaagag atgagagagt gttatttctt	180
gggcaatttt ctattagtgt ttcttatttt ggccagttct tttatttatg tccttgtgac	240
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catgagtga tacctaggag agtgtcagca tgtttctgga aaattggcag agaccaagcc	360
ctgctgcaga ttcgtcaggc caggtgaaag ggccaggcag ttgcagctga tgatgtaaat	420
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aaarwaaaaa aaaactcgag gggggggccc gtaccaaat	519

&lt;210&gt; 77

&lt;211&gt; 389

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 77

ggtcgaccca	cgcgcccggt	ttgccatata	atgagcattt	tgtatacata	aatttatagt	60
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ttgttagggc	catccagtga	tttgttttta	aattttaagt	aatttatctc	tataagttct	360
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<210> 78  
 <211> 823  
 <212> DNA  
 <213> Homo sapiens

<400> 78	
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tgaccacaca	ttaggctgtg
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ctttgcagtg	gggctaggac
taatttgaac	aggtcaaaga
taaaaatagg	cttttttagga
atatttgtcc	ttaaaggggt
gccatgtgcg	gaattcaagt
gtgtacttat	tacagtctta
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	aaaaaaaaa
	aaaaaaaaa
	act
	cga

<210> 79  
 <211> 2455  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (2277)  
 <223> n equals a,t,g, or c

<400> 79	
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accaacgccc	cgcagsggcc
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tggaaccaac	ccagccgacc
ggcagcagga	agaactggac
agaacactgt	agccaacttg
gccctgtgaa	gccctgcttc
ggatatgcaa	gatgctctac
tgcttgcttg	cctggcctgg
ccatcctgtg	gtttctgata
ataaggcctt	taggtccgac
gtcaaatagg	gatctacatc
ggattgcagc	cctgtctaca
tggtggctgg	cttcttcacc
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	ttccacagag
	ctgcttcac
	tgctgccc
	ggagccttcc

```

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&lt;210&gt; 80

&lt;211&gt; 921

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (111)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 80

```

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aagctgttct attcgtttct gcctggtttg gaacaaactg aacacttcca aaggaggcag 180
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atttctagtt tctatatagt gcaatagagc atagattcta taaattctta cttgtctaag 720
acaagtaaat ctgtgttaaa caagtagtaa taaaagttaa ttcaatctaa ttttctctg 780
tggaaaaaaa aaaaaaaaaa t 840

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&lt;210&gt; 81

&lt;211&gt; 678

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 81



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gaattcggca cgctcttggg ggtagtggat gcgggttgag gggtttcagg tgccctgggc      60
tgtcactttg taaaggcttg ccaacctaga ttgagatggg tggtaaagga atcaattaca      120
caatgccaca catttgcttg cttctgctga atgccttagt agtttcatgt ttattgctgg      180
aagccattct cttacagcat ctagtgctgt gtaacgagct accttaaaat gtaaaggctt      240
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gcacttctta aatgatgtca gggttccagg agttaatgtt ccaagagaca ggaagtggat      540
gctgcccata tctttttttt tgtttggttt tttgtttgtt tttttgagat ggagtcttac      600
tctgtacca ctgcactcca gcctgggcaa cagagcgaga ctctgtctca aaaaaaaaaa      660
aaaaaaaaaa aaactcga

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<210> 82  
 <211> 857  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (493)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (562)  
 <223> n equals a,t,g, or c

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<400> 82
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ctaaaccgca tcttactggt attatgctat cagcctgtat tgagagactt tataggtaaa      180
gtccaattta ggctgtttgg tattatctat taaaattaga atgttcatgc tctgtaacct      240
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acattgaagg gcntacgaga tacaaggagt ctgtccttag ctctgccctt tggactgttg      540
tctgaaggct aaagaagaga gnacaaagaa agcttgcatt gggaggctga ggtgggagga      600
tcacttgagc ttaggagttt gagaccagcc tgggcaacat agggagactg cacctctata      660
agaaatttta aaaattagcc gggttggcag cgtgctcttg tgggtcccagc cgcttgaaaa      720
gctgaggtgg gagaatcgcg tgagcctggg aggtcgaggg tgcagtgcac cgtgattatg      780
ccactgcact ccagcttggc aacattgact gtctcaaaaa gattatatat ctctaaaaaa      840
aaaaaaaaaa aaactcga

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<210> 83  
 <211> 1977  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (664)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (716)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (1319)

<223> n equals a,t,g, or c

<400> 83

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caggctctcg	ccttgatcgt	gttctcctgc	atctatgggtg	agggctacag	caatgcccac	180
gagtctaagc	agatgtactg	cgtgttcaac	cgcaacgagg	atgcctgccg	ctatggcagt	240
gccatcgggg	tgctggcctt	cctggcctcg	gccttcttct	tggtggtcga	cgcgtatttc	300
ccccagatca	gcaacgccac	tgaccgcaag	tacctgggtca	ttggtgacct	gctcttctca	360
ggatatctgc	tgtggcacct	ccatttgatc	ttgggggagg	cattaactct	agggttccgc	420
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atgccccggc	tgggatgctg	tttgagagc	gaataaatgt	ttctcattc	aaaaaaaaaa	1920
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<210> 84

<211> 1149

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (837)

<223> n equals a,t,g, or c

<400> 84

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aaggmaatt	ttgtttcaac	agtttggaag	tcatctgtgg	gtccagcttg	actttggagg	180
aataagaaga	tacttctaga	gtatgggaat	gattccagat	aatttctggg	atttgaatct	240
acttgagttt	aagggcctgg	gacctaattt	ggttttagtat	agaatttgaa	gaattaatct	300
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agggcggcc 1149

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&lt;210&gt; 85

&lt;211&gt; 767

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 85

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ccaacgtaaa tatgcttcgg caaaaaaaaa aaaaaaaaag ggcggcc 767

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&lt;210&gt; 86

&lt;211&gt; 728

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 86

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taaattatgt atacataata tataaccaa ttgaaacagt tttaaatatt ggtttgactg 660
gaaattcaaa atccatatat taatttttgt agtaaaagt tatgtaaaaa aaaaaaaaaa 720
gggcggcc 728

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&lt;210&gt; 87

&lt;211&gt; 735

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (376)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 87

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aaaataactt taaactgatt taatatttca tatttacatt atatgaaaat caattacatt	120
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ttttatgtag attttcctcc catgaacatg agtaaataaa tctgtttctt gaatggattg	660
tggttgcatt taaagctctg taataattct aataaattta ctctatagaa aaaaaaaaaa	720
aaaaaaaaa ctcga	735

&lt;210&gt; 88

&lt;211&gt; 889

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (117)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (292)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (341)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 88

tgtaggtta attattgctt cacatgtggt cacggtttga aaacttattt tggggggagt	60
ataaagtaga atacagagat tccttgctca tagtcctac tgctatcggg gaacaancct	120
tgagggtgag aacgtggatt gattcttgat tgatagtggg gattccatta tctgtatttg	180
gcagttatgg cctgctgcgg tgtatagaag cttctttcca ttcattttcc cgaattttca	240
tactgctcaa ggaacagttg ggggggaatg ggcagaaggt tgggcacttg angtatattga	300
gctatcggtta ataactgact ttttagggcg cacagatttg nagtagagcc atggtagtag	360
ttagtaccaa tgggtttttg ctgcttctac tctttcttaa cagaaaaagt ggattgtgtt	420
catataggaa agcagttcac agactgtctt cctgccctc cgcaccacaa gctggaccta	480
gaatcaagtg tgactttaa tggggaaagc tgtgttacag ttgtgcttaa gccactgctg	540
tggcttaacc tcacctatgc ataagaattt gctcgtggct ggccggggcg ggtggctcga	600
gcctgtaatc ccagcacttt gggaggctga ggcgggcgga tcacgaggtc aggagattgg	660
gaccatcgtg gctaacacgg tgaagccccg tctctactaa aaatacaaaa aaaattagcc	720
gggcgtggtg gcggggcgcg ctagtccac tactgagtc caggctgaag caggagaatg	780
gtgtgaacct aggaggcgga sttgcarcga gccgagatcc tgctactgca ctccagcctg	840
ggcgaagcga gactctgtct caaaaaaaaa aaaaaaaaaa aaaactcga	889

<210> 89  
 <211> 569  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (1)  
 <223> n equals a,t,g, or c

<400> 89	
ntaaggtggt gattctggat cacgggatac cattcctgtc macaccccgga ccaggggcta	60
gaaaatttgt ttgagatttt tatatcatct tgtcaaattg cttcagttgt aaatgtgaaa	120
aatgggctgg ggaaaggagg tgggtgccct aattgtttta cttgttaact tgttcttgtg	180
ccccgggca cttggccttt gtctgtcttc agtgtcttcc ctttgacatg ggaaaggagt	240
tgtggccaaa atccccatct tcttgacact caacgtctgt ggctcagggc tggggtggca	300
gagggaggcc ttcaccttat atctgtgttg ttatccaggg ctccagactt cctcctctgc	360
ctgccccact gcacctctc ccccttatct atctccttct cggctcccca gccagtcctt	420
ggcttcttgt cccctcctgg ggtcatccct ccactctgac tctgactatg gcagcagaac	480
accaggcctg gccagtgga tttcatggtg atcattaaaa aagaaaaatc gcaacaaaaa	540
aaaaaaaaa aaaaaaaaaa aaaactcga	569

<210> 90  
 <211> 334  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (321)  
 <223> n equals a,t,g, or c

<400> 90	
agaaaatgaa caaactagtg agaaacattg taaacatata gtgtagatga taactctgaa	60
cttaagtaca agataatgat gaattattctg ctgcttaagt atatcttaga aatattaatt	120
cttagtgaaa atcttaacct attcaacatc acttatggta agtataactt atttttccta	180
tacaggtatt aaatatataa tttatatgcc agtcacattt cctcacacta aataaggcag	240
cagacacata tatttaatat catgggtatg catttttagt tctaaaacct aaggtatgtg	300
gattttcttaa agccatatct naaatatttt cacc	334

<210> 91  
 <211> 795  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (3)  
 <223> n equals a,t,g, or c

<400> 91	
cgnaccattt tttttttttt gaatatcatc agcttacttg actggcaagg gcagaagctg	60
gggttgccct gaactctgcc aaacaaatat caaagtgtat ttaatagtta aatttggcc	120
ctttcccttc ttgtgcacc catgtgtgca cttaaccccc aggagtatt tattatcttt	180
ttgttaaagt caggctcatt tggggtaatg tgatgactgt ttaggtttac atgacctcc	240
tctcctttcc ctaccccaaa atatgtatat atacatata aaaatatgta tatattttac	300

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ctatataaaa tatatatata tacacatata tgtatctata ttcctttggt tctttgcctg 360
cttataactgg ccataaaaaga gggagctgcc ttcaatgtat aaagtataag aagagtgcc 420
gggaatgccca taatggaggc ttttgatct gaatttggac catttcta aagagaacat 480
gagtttgcctc agccctttcc tcacaagagg gagggcccg gttcccaga cttctccacg 540
cgctggctcc ataaaggcca gctttggccr ggctgccaca ggggcctgag gagctcactc 600
tgggcctacc tggtttcagt tagagggtcc tcctgttatt ttccattta aaaagtatgt 660
cctcagaaaa ctgtactgga aggatgggtg gcaggaactt gtatagtcca gcttccaaca 720
ctttggaaca gattaaaaag ggaatctttt aaataaaaac gtataaaaat aaaaaaaaaa 780
aaaaaaaaagg cgcc 795

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<210> 92
<211> 577
<212> DNA
<213> Homo sapiens

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<400> 92
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tccacatttt gggatgtctg ttgctgctct tccttggggg ggaagagca ctggagccct 180
tctctggtct ttgtgcttct ttacatgatg tgagacctat agtaaacccc ttaacctcct 240
tcagcctcat ttattagaga gagagagaaa aaaaaagggt attttaaaaa aatctgtttt 300
cgccagggtg cagtggctca tgctgtaat ccagcactt tgggaggccg aggcagggtg 360
atcacctgag gtcaggagtt cgagaccagt ctggctaaca tggtgaaacc ctgtcactac 420
taaaaatacm aaaaaatcag ctactcggga ggctgaggca ggagaatcct atgaaaacgg 480
gaggcagagg ttgcagtgag ccgagatcgt gccattgcac tctagcctgg gcaatgagca 540
aaactttgtc tcaaaaaaaaa aaaaaaaaaa actcgta 577

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<210> 93
<211> 968
<212> DNA
<213> Homo sapiens

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<220>
<221> misc feature
<222> (904)
<223> n equals a,t,g, or c

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<220>
<221> misc feature
<222> (907)
<223> n equals a,t,g, or c

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<400> 93
gaattcggca cgagcttact ttcaactacc gcctgtcctt cctgacacct caccatgtgt 60
acgggaaaaat gtgcccgctg tgtggggctc tcctcatta ccctctgcct cgtctgcatt 120
gtggccaacg ccctcctgct ggtacctaata ggggagacct cctggaccaa caccaacct 180
ctcagcttgc aagtctggct catgggcggc ttcataggcg ggggcctaata ggtactgtgt 240
ccagggtatg cagccgttcg ggcagggggc aagggtgctg gtggtgctgg gtgctgtgga 300
aaccgctgca ggatgtgcg ctcggtcttc tcctcgcgct tcggggtgct tgggtgccatc 360
tactgcctct cgtgtgtcgg agctgggctc cgaatggag ccagatgctt aatgaacggc 420
gagtggggct accacttcga agacaccg cgagcttact tgctcaaccg cactctatgg 480
gatcgggtcg aggcgcccc tcgctgggtc ccctggaatg tgacgctctt ctcgctgctg 540
gtggccgct cctgcctgga gatagtactg tgtgggatcc agctggtgaa cgcgaccatt 600
ggtgtcttct gcggcgattg caggaaaaaa caggacacac ctactgagg ctccactgac 660
cgccgggtta cacctgtccc ttctggagc ctactccct tgctcgctag aataaactgc 720
tttgcgctct caaaaaaaaa aaaaaaaaaa tcgagggggg gcccggtacc caattcgccc 780
tatagttagt cgtattacaa ttactggcc gtcgttttac aacgtcgtga ctgggaaaaa 840
cctggcggtta ccaacttaa tcgccttgca gcacatcccc ctttcgcag ctggcgtaat 900

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aacnaanaag cccgcaccga tcgcccttcc caacagttgc gcagcctgaa tggcgaatgg 960  
 caaattgt 968

<210> 94  
 <211> 553  
 <212> DNA  
 <213> Homo sapiens

<400> 94  
 gaattcggca cgagtcctta aacagttaaa atgtcacagc tgtttcttat aatgcttaca 60  
 ttcataatttc taaataacat gtttataatg catctaactt ccttccatgg aaaaagagta 120  
 tttggctttt taaaccaatc gagtcacatg catgctttcc cccttccacg ttggactaca 180  
 tcaatattta gtgttagtat ttttataaat agataaatat tgttcgcaaa ttttatttgc 240  
 tgtctattgc tgtgtaacaa attcctccaa aattattggc tttaaacaac atttattatc 300  
 ccatagtttc tatgagttga gaatctaagc aggtcttagct ggggtccacta gctcggggtc 360  
 tctcacaagg ccacagatca aggtgttggc cagtgggttg tgcccttagt ccagctact 420  
 tgggaggctg aggcaggagg atcacttgaa cccagtagtt caaggctgca gtgagcwakg 480  
 gttacaccac tgcactccar cctgggtgac agagcaagat gccatctctt aaaaaaaaaa 540  
 aaaaaaaact cga 553

<210> 95  
 <211> 968  
 <212> DNA  
 <213> Homo sapiens

<400> 95  
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 aatccatttg ctaaaggctt ccgagactcc gggcgcaaca gaatgggttt ggaagccttg 120  
 gtggaatcat atgcattctg gcgaccatca ctacggactc tgaccttga agatatccct 180  
 ggaattccca agcaaggcaa tgcaagttcc tccaccttgc tccaagtact gggaaatggcg 240  
 ttctgtccac tcacctcac cttttgtctg gctcctcttg ctctctctct gccttccatc 300  
 tggggcccaa caccagccag ctgtgtagtc tggcccttgc tgactattct gcctgtgcc 360  
 gctcaggcct caccctcaac cgatacagca catctttggc agagacctac aacaggctca 420  
 ccaaccaggc tgggtgagacc tttgccccgc ccaggactcc ctctatgtg ggcgtgagca 480  
 gcagcacctc cgtgaacatg tccatgggtg gcactgatgg ggacaccttc agctgcccac 540  
 agaccagctt atccatgcag atttcgggaa tgtccccca gctccagtat atcatgccat 600  
 caccctccag caatgccttc gccactaacc agaccatca gggttcctat aatactttta 660  
 gattacacag cccctgtgca ctatatggat ataacttctc cacatcyccc aaactggctg 720  
 ccagtcctga gaaaattgtt tcttcccaag gaagtttctt ggggtcctca ccgagtggga 780  
 ccatgacgga tcggcagatg ttgccccctg tggaaggagt gcacctgctt agcatggggg 840  
 tcagcagagt ttctttgact ctaggaccct aggaagctta actctgtcat catctcaagt 900  
 atctgcacat atggctctgat gaagccttta aagttaaatg aacatttggg atctgtctaa 960  
 acatattt 968

<210> 96  
 <211> 697  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (19)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (50)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (57)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (662)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (680)

<223> n equals a,t,g, or c

<220>

<221> misc feature

<222> (690)

<223> n equals a,t,g, or c

<400> 96

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acactagtgg atccaaagaa ttccggcacga ggccacatcc caccggccct tacactgtgg	120
tgctcagcag catccggctt catgggggga cttgaaccct gcagcaggct cctgctcctg	180
cctctcctgc tggctgtagg tctccgtcct gtccaggccc agggccagag cgattgcagt	240
tgctctacgg tgagcccggg cgtgctggca gggatcgtga tgggagacct ggtgctgaca	300
gtgctcattg ccctggccgt gtacttctctg ggccggctgg tccctcgggg gcgaggggct	360
gcggaggcga cccggaaaca gcgtatcact gagaccgagt cgccttatca ggagctccag	420
ggtcagaggt cggatgtcta cagcgacctc aacacacaga ggccgtatta caaatgagcc	480
cgaatcatga cagtcagcaa catgatacct ggatccagcc attcttgaag cccaccctgc	540
acctcattcc aactcctacc gcgatacaga cccacagagt gccatccctg agagaccaga	600
ccgctcccca atactctcct aaaataaaca tgaagcacia aaaaaaaaaa aaaaaaaact	660
cngggggggg gcccggttan ccaatttggg cctaaag	697

<210> 97

<211> 866

<212> DNA

<213> Homo sapiens

<400> 97

ttttagtcca ttattctctt ctattaagag aaattcactg ttaaaaaatt gtttccatt	60
tccgtatctg aaataatgac tgtagttgag gtgatcttgc cctgggtctg aaatcatact	120
tccaaaccaa aaaggacttt gaatacaaaa cttttaagaa atcttgtatg aatacaagct	180
atatctgaaa aattgtgttt tataatattg atgcctagtt ttgcccagc ccatctgcag	240
tgtggttact atgcaaagaa tgctggtgtt gctgtttttt tttttttctt tgttggctat	300
taaccacgag gagacaatat gtggctatgg tagtacttgg aagttctagc attacacaga	360
ctagcttcca tttctctcat agaggctcatt ttggcattta aaacacatac ttttagaaaa	420
cagatttgga tgatgtaaa cacagggtta atccaccaca ctctggatgc tagagctgtt	480
gacaaagtca tgctttgcag atttttaaat aaactttttg ttactcttac agcttgggtat	540
tttccctctc tttttttttt acctcctcta aataaacctc tttgttaaat aattgatgtt	600
tctggatcat agaaaaatag aagtttaaaa tacagaatat ttccaagcta actacaaatc	660
tgatgacagt tttttgagtg tgcacttttc cttttatttc ttaggtcctt tttggtcctt	720
tgcaaacata gtaagattcc atatttgtgt cccaactgtg gtaatatgtc tgacttctta	780
ctggaaaaca gtcagctcta ggtagcattt cttctgtgtg gtatttaagt taaattatta	840
ccaaaaaaaa aaaaaaaaaagg gcggcc	866



<210> 98  
 <211> 1368  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (637)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (1140)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (1170)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (1286)  
 <223> n equals a,t,g, or c

<400> 98  
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 ggcttcctca tcctgggcgg cctgctgctc aactgctgcg tgtgtgccgc actcatgagg 120  
 cccctgggtg tcacggccca gccgggcycg gggccgccgc gacctccccg gcgcctgcwa 180  
 gacctgagcg tcttcgggga ccgcggtctt gtgctttacg ccgtggccgc ctcggtcatg 240  
 gtgctggggc tcttcgtccc gcccggtgtc gtggtgagct acgccaagga cctggggcgtg 300  
 cccgacacca aggcgcctt cctgctcacc atcctgggct tcattgacat cttcgcgcg 360  
 ccggccgcgg gcttcgtggc ggggcttggg aaggtgcggc cctactccgt ctacctcttc 420  
 agcttctcca tgttcttcaa cggcctcgcg gacctggcgg gctctacggc gggcgactac 480  
 ggcggcctcg tggctctctg catcttcttt ggcatctcct acggcatggt gggggccctg 540  
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 cctgaggtgg gcgccgcgga ggaggagaag ctccacaagc ctccctgcaga ctcggggggtg 840  
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 atgtcaagg acctggaac ccatgcttcg agacaacgtg actttaatgg gaagggtggg 1260  
 tgggcgcgag acaggctggc agggcnggtg ctgctggggc ccctctccag cccgtcctac 1320  
 cctgggctca catggggcct gtgcccaccc ctcttgagtg tcttgggg 1368

<210> 99  
 <211> 613  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (25)  
 <223> n equals a,t,g, or c

&lt;400&gt; 99

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gttgacgac	tcccagtaga	ccaggagctc	cgggaggcag	ggccggcccc	acgtcctctg	120
cgcaccaccc	tgagttggat	cctctgtgcg	ccaccctga	gttgatcca	gggctagctg	180
ctgttgacct	ccccactccc	acgtgcctc	cctgcctgca	gccatgacgc	ccctgctcac	240
cctgatcctg	gtggctcctca	tgggcttacc	tctggcccag	gccttggaact	gccacgtgtg	300
tgccacaac	ggagacaact	gcttcaaccc	catgcgctgc	ccggctatgg	ttgcctactg	360
catgaccacg	cgcacctact	acacccccac	caggatgaag	gtcagtaagt	cctgcgtgcc	420
ccgctgcttc	gagactgtgt	atgatggcta	ctccaagcac	gcgtccacca	cctcctgctg	480
ccagtacgac	ctctgcaacg	gcaccggcct	tgccaccccg	gccaccctgg	ccctggcccc	540
catcctctctg	gccaccctct	gggtctctct	ctaaagcccc	cgaggcagac	ccactcaaga	600
acaaagctct	cga					613

&lt;210&gt; 100

&lt;211&gt; 685

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 100

gaattcggca	cgagcctcag	ccaccccagt	agctaggact	atagacacaa	gctagccttt	60
ttatacttac	tgttttcatc	aaatgtcttt	ttccaactag	ttccaacct	gtctttgtat	120
ttgaagtga	tctattgtag	atagtccagt	gttgctttta	aagtgcctac	tccatttgtg	180
tttagtatgt	tgacatgggt	ggatttagat	ctactatttt	gctttctgtt	tttattcctg	240
ttttatcctt	tttacttctt	acagcttaat	gaattttggg	gggggaatcc	attttaattc	300
tctcttgggt	ttttagctac	atcttcttta	ggattgcact	agagattaca	atatacattc	360
ttaacgtctc	acccttttgc	ctggggcggt	ggctcatgcc	tgtaatccca	gcactttggg	420
aggctgaggt	gggtggattg	cctgagctca	ggagtccag	accggcctag	gcaacatggg	480
gaaacctgt	ctctatgaaa	aatacagaaa	cattagctgg	ttgtggtggc	acacacctgt	540
agtccagct	acttgggagg	ctgaggtggg	aggatccctt	gagcctggga	ggttgaggct	600
gcagttagct	gagatcatac	cactgcattc	tagcctgggt	gacagagtga	gatgctgtct	660
ccaaaaaaaa	aaaaaaaaaa	ctcga				685

&lt;210&gt; 101

&lt;211&gt; 646

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 101

tcgaccacg	cgtccgataa	ctttttcaag	caatatcagt	gagtgggtcc	catcgacagg	60
gttccaggac	ctggaacact	ttaacagaag	gaaatgccga	agcagcttgc	acagttgctt	120
tacagacttc	caagaggctg	attctggctt	caagatggag	ccttgaggat	ggtttttttt	180
tttttttttt	ttcttccctc	aaagaacctg	cggttgcgct	ttgtgtgttt	tgtttttggt	240
ttccatttgg	gggccccatg	ggaaagagct	tctgaactct	ttcctttatg	aactcccact	300
gtgttctctat	aaaggccctt	ttctttctta	gtgttgtaag	ttacattttc	attatgcccc	360
atcacatctt	ctttactgta	aaaatattaa	aaagctgttt	ccaagtggga	cagctaataga	420
agctctaatt	attgcagaca	tatttttgag	atgtaaaaaa	aaaaatttaa	agttaaatga	480
taagtcttag	aggcgagtga	ggaataaaat	ggatgtaaac	atttacatgg	gatgcattag	540
aattctgctg	tgtgtactgt	cttttggttg	aaacaaatta	tgaacagtga	ctaataataa	600
aaagtcaata	cccaawraaa	aaaaaaaaaa	aaaaaaaaag	gcggcc		646

&lt;210&gt; 102

&lt;211&gt; 826

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (726)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 102

ggtcgaccca	cgcgctcggc	tccctttgtt	ttggtggcag	ccttcttgtg	ctgtatactt	60
gttccttagg	gtgtataata	atatgtgcac	tagagtgtcta	ggtagccctac	cacattgctg	120
ggaccttgcc	acactgtgc	agccttccag	taggatatgg	gggaatgtca	gtgaggctcc	180
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gaccagcat	gagctccctc	tttggagcag	tgctgtctga	gactccaggc	agctccgtgt	360
attagtctca	ggacctgcaa	aggcctaggg	gctctttttg	ggtaggactg	caggagtctc	420
catggtggga	atgtgaacca	ctggaaatct	ctcatttacc	atttccctgt	actggagatg	480
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gcataaggca	ttttctgtca	cttctctgct	gaactctagt	gttctttctt	agaggctgta	600
ctcaaagttt	cattatccat	tcagtatttt	tattcttctt	tgtggagggt	gcaagtgtca	660
ggtgcctcta	gtcaatcatc	ttgaagcccc	ctgttatgtt	aaagtcttta	atggaaaaag	720
aagacnacat	gcatgaccag	gcagatactt	tgagcagagt	cataggaact	gctaaaaaaa	780
aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaag	gcggcc		826

&lt;210&gt; 103

&lt;211&gt; 586

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 103

gaattcggca	cgagggtggct	atcagatttg	gggttctact	ctatgagact	tttaagtcac	60
tatgcaattt	ctttattttw	atttttttga	caagaagtct	ggagcatgat	tacattatgc	120
attttcttac	tctttaaagt	atgtgtggg	ataatccttc	attatttgat	tggcaaaaat	180
atatatgttt	atagtgtgta	acatgggtgat	tggatatatg	tacacattgt	ggaacagcta	240
aatcaagcta	ataacaaatc	agttacctca	catacttatt	ttgtgggtgaa	aacatgtaaa	300
atccactctc	ttagcaattt	tcaagcatcc	aatacattgt	tawtaactgt	agtcaccatg	360
ttatacaata	gatctcttga	acttattctt	cctgtctaac	taaaattttg	tattccttga	420
tcaacatcta	cccaatccct	cactgttctc	cagcctkgat	aactaccatt	ctactctctg	480
cttctatgaa	tttgactttt	ttttttttta	gattccacat	atgtgagatc	gcgcagtatt	540
tgtctttctg	tgcttggtct	atttcactta	atataaagtc	cctcga		586

&lt;210&gt; 104

&lt;211&gt; 628

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 104

tacagcagtt	taaaaagcag	tgtctttctt	tgagagacag	gaagtctagt	gaagagccag	60
tatttttagg	atagataatg	aaagaggctg	tcatttcaga	cattttaatc	ctctgaaaga	120
atacaaaaga	aaaaaaaaag	aaaacaaatc	tttcagaatt	gtttgaagta	agaacaagac	180
aagaggaggt	gattggtgtg	ttactgttct	acgaaaaagg	agaaaaagct	tcatgaaatc	240
gccattcagc	aaggacagaa	ctggagatgg	cttctctttt	acaaagaaat	ctctgtccca	300
ggctttcagt	ctgttttggtg	ttcatacaag	tgtttgtgtg	ttgtgtggaa	ggcgggggaa	360
ggcgggtgaa	ggcgggtcctg	ttcaggggccc	cctttggtga	acacagcagg	caaaatactc	420
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gcctttgaat	agaagctgac	acgtagcagc	cagctgaaca	agtatttaac	gaggagcaac	540
acaactccaa	gaagggctcc	ttagtgtatt	gtcaagttgc	tcagccttg	tgagatggaa	600
aaaaaaaaaa	aaaaaaaaaa	gggcggcc				628

&lt;210&gt; 105

&lt;211&gt; 558

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 105

agctctaata	ttactcactw	tgaaggsaaa	gctggatacy	cctggcaggt	accggttccg	60
ggrattcccg	ggccccatca	caccctatgg	gggagagcga	atgttacagg	aggctttctg	120
gtgcctcgtg	cacatggact	gtgcatgtgg	attttgccta	aggtcagcct	tatatgcatt	180
gtggaactag	ggtatggaaa	accatgaaac	atgattatth	tcttctagca	tgctctgtcta	240
tgacttcaac	tggtgtgtatt	ctttgtactt	tataatctac	attatcatta	atacctacat	300
cttcaagtct	gtctttctgg	ccatggtgta	cagcaattat	aggaagcatt	ttcacatact	360
gtgtgtgtgt	gtgtgtgtgt	tttgtagtga	tgaacagaac	ttgttattta	cccaattcta	420
ttatctatca	taatagtaaa	ttagctacta	taatagacaa	aagtatgact	ctcagttaaa	480
taagagattt	tttaaaaact	tggtacaaaa	aaaaaaaaaa	aaararaaar	aaaaaaaaaa	540
aaaaaaaaaa	gggcggcc					558

&lt;210&gt; 106

&lt;211&gt; 756

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (230)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (755)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 106

gaattccaat	gtccacaggt	gatgggagag	atgctgagaa	agggtggcca	gtgagtgagg	60
aggaaaacca	gaggagtgtg	tatcctgggt	accctgaatg	tgatgagcga	caagctgtcc	120
cccagcactg	tgccattgct	tctcccagtt	ctcttcaaag	tcaccatcct	gcttcagcgt	180
gtgtgtcccg	aagatagccc	ttctctttct	gtgcttccag	aatccgtagn	cagggaaatag	240
gaatacatgg	acaagtagca	tgcatgtcag	tgagaatgta	taacaacaga	tgactctggg	300
gaccaaaatc	aaatggggcc	agctacaaaag	agggcaggaa	atccccacag	gtgattttac	360
tgtgaggaat	tttatgaggt	tcagcatcat	atattgttag	gagaaaatgc	tgttttgata	420
agcagagata	tgagaaaagt	aaacgggaac	tatgatttag	agatctcatc	tgrrtacttt	480
gtcctattcy	cagtttwatt	actaaagagc	agtaaaagcca	aggagaaaat	agtaaaagatt	540
agatgaatgg	ttagcatgtg	aaacctgaaa	ggaaccagag	tgatttccct	cgaggaacaa	600
atgcacttct	cttacatatg	aaagatgatg	tgttctgtgt	tcccatagaa	tctagggaaa	660
gaaaaagtga	gcagatactc	tgatatgagc	aatataactt	agggtgaaaa	aaaaaaggaa	720
ttcgatatca	agcttatcga	taccgtcgac	ctcgna			756

&lt;210&gt; 107

&lt;211&gt; 1146

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 107

cccgtccaca	atgcagcaga	ctcttcccaa	ggccacctag	caagcaaggt	tgatcggatc	60
atctaaaactg	gcgcctcct	gaatatthca	ctgaatcctg	gcgttcatgt	tgaagcagac	120
aaaatgagaa	aggaggagg	cattgctcac	ctctcaatag	cttttttctg	tcaagttcta	180
tgtctttatc	agctcttgcc	tgtgatttta	ccccaattca	accttgggag	tggaagaat	240
atgaacagat	aacccttggc	ctaacagctc	catcaaacct	ccttgagagc	aactacctag	300
gccaggctag	tgagtgtctt	gtgaggaagc	tggtcagaag	gttccctcaa	ctccttcctg	360
gtcctcctgg	acactgcaga	aaagacttag	gggatcccca	gcagaggcca	attgctctcc	420

ttccttcctt	gccccaccag	gaaaggaata	acgtccacag	acttgaagca	gatagtgaag	480
tagatctgtg	agaggttcta	ggtacttagt	gtgtagactt	tgacgaatat	ttctcaagtt	540
gggagccctt	gttaaaaatg	atgtttaagg	gagtggttgg	ggggaagatg	aaggcatgga	600
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tgacagaata	aataaagtgg	atgctacccc	actccagaat	caaaagcaat	ttaattaaag	720
tctcttaagt	tgtaaagagt	tttaaatgat	ccgtgttgaa	ggcgaatsct	gcyaaatgca	780
gtgggtctga	cgtcagctgc	cgggcctggg	ctgggaggcc	atttgctatt	ctgtttaagg	840
caggctggat	tgtcttattt	tggaaccagc	ttggtggggg	gtttgctttg	ctactgcttc	900
tgagccctga	gcttcaaagg	ctgaaattaa	tggtgaacaa	aattgtgcgg	ctctggccat	960
cccattgctg	caagcccatt	gagggttatc	attaagtaaa	gaaataaaga	gggggaaaaa	1020
agcctgcctg	ttccaaaaac	ctcatcagat	aatgacctca	gtgattgggt	tttcattacc	1080
aaacagcatc	cagagattat	caacccatag	aagaagggag	gggaaaaaaa	aaaaaaaaaa	1140
aaattc						1146

<210> 108  
 <211> 775  
 <212> DNA  
 <213> Homo sapiens

<400> 108						
tgcacccacg	cgctccgaaaa	aggaaatgat	acatgtcttg	acattttctat	tgcagtwtta	60
catcttaatt	tctaaggcca	aaggtgatgt	ttcccagttc	gtaaagtctc	gagagtacta	120
atgctatcaa	aagtaattaa	tttcaagtgt	aaataagacc	aaacaaaaac	gatcagatgc	180
gacattgtct	cataaacatg	atagactatt	aaatcacttt	gtgttttttg	gaaacagcta	240
taactattaa	tatatacagt	aatctagtaa	atttccttca	gatatgctat	tgccgataca	300
acagatcatc	tattgtcaca	agctaaccat	tatcctaaca	aaatggcgga	atacagcaag	360
acataagagt	aaaaagaaa	aagatgagct	gatattaaaa	catgaacttc	aattgaaaaa	420
atgaaaaaat	aggttaatac	tcaaaagagc	tgctgcagaa	gaatccaatt	ttcctgaacg	480
aagttcttct	gaagtctttc	ttgtagatga	gactctaaaa	tgtgacattt	cactgttacc	540
kgaargrca	atattacagg	ttgtatgaa	ttcagtatac	attatatact	ataatctgcc	600
aagtgtggtg	gtgcatgcct	gtaatcccag	ctgcttgagg	ggctgagaca	ggagaattgc	660
ttgaaccag	gaggcagagg	ttgcagtga	ccgagatcac	accattgcac	tccagcctgg	720
gcgacaatag	caaaactcca	tctcaaaaaa	aaaaaaaaaa	aaaaaaagg	cggcc	775

<210> 109  
 <211> 911  
 <212> DNA  
 <213> Homo sapiens

<400> 109						
gaattcggca	cgagacgaca	atggggaacg	cggtgtttcc	cacctcttgt	gggtagaaag	60
cagtcctgct	tgaggaggcg	agaaggcaaa	gccagggcag	ggcgttgctg	tggaagcgt	120
tcggtgaaag	crggtttcga	cgcttaggag	ggccgaggga	gaagattcca	ccagcattgt	180
ccttgcttca	agtttttaga	tgtctgaact	ttcagctttc	atgttttcaa	ccatcatttt	240
tttaattgga	caacctacat	cttgttttta	aaagaagtag	cctcaaatta	aactcctaaa	300
ctctgatgcc	ctggggatga	gaacaactag	ctkggatctc	gtgccgtgta	atcaatgttt	360
cattccgctg	cctccatcat	gtaatagaat	cgcttccaga	aaggcagtta	actggaagca	420
gcagaggctc	ccagccgtga	gaggactgct	caacaatgcc	ccccatcgcc	gccccccac	480
ccctcgacac	ccttggtgtt	tcccctctga	ggggcccaag	ggttatggct	ttcatgtcta	540
ggtgtgggga	cagaggaggg	agaggcagat	ccygggccc	gagaggatgg	ccctggctcg	600
aatctggagt	aattaatgcc	cacccaaaga	aaaggccctg	cccaggtcca	atgttgctct	660
agatctgatg	atgctgctat	ttacaaaaca	ctgatcgctc	gaaagcttga	atctgttcct	720
cctcgaaatg	ccctgtagat	gcctgacctc	caccgtacct	ccacatcact	attcatgtcc	780
ttctaggaaa	atgtgcacat	gcctcacgca	ctatgtggga	agggcgtgtt	tttaatttaa	840
taaagtgtgt	caccattagc	catamraaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	900
aaaactcgta	g					911

<210> 110  
 <211> 456  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (456)  
 <223> n equals a,t,g, or c

<400> 110  
 gaattcggca tgagctttct ttctcctgca ggcatggaa atacagtccc agctggcaac 60  
 accagccagc agcacagccc ggaatcctgc tcctgacctg caccatcccc accagccac 120  
 gatagaacgt ttttgtaggc attcctcctc atgggagagg atagagtaca tgcgagtttt 180  
 tgctctcctc ccaccctttc acaagagcac tgtgctttct tttcttctct ttttcctttc 240  
 tttttttttt tttaggcagg gtcttgctgt gtcascagg ctggaatgca gtggtgcaat 300  
 catagctcac tgcagccttg acctcctgga ctcaagcaat cctcctgcct taacctccca 360  
 gctactcagg agaccgagac aggaggacca cttgagccca ggaggttgag gctgcagtga 420  
 gccgagattg caccactgca mtccagcctg gggaan 456

<210> 111  
 <211> 554  
 <212> DNA  
 <213> Homo sapiens

<400> 111  
 gaattcggca cgagcctcca cctcccagggt tcaagagatt ctcctgcctc agcctcctga 60  
 gtagctggga ttacaggcgt gcaccaccac acgttgctat tttttgtact ttaagtagag 120  
 acggagtttt gccacattgg ccaggctgggt ctcaaactcc tgacctcaag tgatccaccc 180  
 accttggcct cccaaggtgc tgggattaca ggcatgagcc actgtgcctg gtcctcattta 240  
 caactatttc tatcattata atgcaggggc tctcaaact gagcatgcct cagaatcccc 300  
 cagagggctg tgcgcacaga ctgctggacc tttcccagc ttctgattcc gtccctccag 360  
 agtggggctc gaagattgcc tttgaggtga rgctgcgggt cgggggcacg tctgagaact 420  
 gctgcagagg tgartgctgt ggctctgtct gcattccccc tggaagactg argcaccagg 480  
 tgtgctgggt ctaacagacc acaagtccct cctggacact gcccttctct gaagggagct 540  
 gccctctcac tcga 554

<210> 112  
 <211> 722  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (2)  
 <223> n equals a,t,g, or c

<400> 112  
 gnaattcggc acgagaaaaa tttacgggta acactgaggg gtgggggtgga aagttttgat 60  
 cataaagtgg tcaccaacaa gggcacttct gaggtgctaa tgatgttctg ttttctgac 120  
 tgggtcgtgg tgacattcac atattcatta aattgtacat ttgttttaca taagtttatt 180  
 atatttccta attttaaaaa agttaaaagg aggaggaaaa agttggttat gaaagtgtaa 240  
 ccattcttcc aaaatatcaa ttaaaacaca tctgaattaa gaggtaaaa atatcaaaga 300  
 ttgacagaaa acaaaagctc tgaatgata tttccagcct aagaacagtc gttgcttttg 360  
 ttggtttagg aagttttgtt ctcctgaact aatgttcaaa atgaaaaaaa gtcacctggg 420  
 ccaggagcag agggccacac ctgtaatccc agcactttgg gagggcgarg tgggtggatc 480  
 acaaggtcag gagatcgaga ccattcctgggt taacgtgggt aaaccccatc tctacaaaaa 540  
 tacaaaaaat tagctgggct tagcgggtggg catctgtagc ccagctact cgggagattg 600

aggcaggaga atggcatgaa cctgggaggt agagcttgca gtgagccgag attgcgccac 660  
 tgtaccagcc taggtgacag agcgagactc cgtctcaaaa aaaaaaaaaa aaaaaaactc 720  
 ga 722

<210> 113  
 <211> 931  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (930)  
 <223> n equals a,t,g, or c

<400> 113  
 gaattcggca cgagaaccag atgtttttcc acacagaatg ctagttcttt aagacacagg 60  
 ctgggtgaca tgtttcccta gagtgacaat atttccttat agtgacattt tccttgactg 120  
 gctccatgca gaataggagg atatagaata ggaggagaag gttcttgctg tggcacctgg 180  
 agtggctactt ggtgcacgcc aggtgctaga caatgtgtgt gacaaggatg cacgtgaaat 240  
 gccccccccc gagtgccctca gtgactgcag taaagtggcc cttgtcatgg tcctcttcct 300  
 ctttctgcat cagtcttcat gctgggcggc atgaagagag aaacaaaaac cacctttctt 360  
 gccagggtct tagtaccatt tgctgctctt atctttcaag taaggagagaa catctaagaa 420  
 acttatcacc gtattcattc tagactgtta gggrtttaac tcttcaccta cttccctgag 480  
 tgggtctgggc tggargttca gagctaartg ggctgggtgt aaatcaggat tccgtccctc 540  
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 aaaattgggc atgctaatac ttttccatct ccttcccagg gttcacagga ttaaatgaaa 660  
 ttattaacac aaagtctctg gcctggtagg gggcatgtac gtggccaccg tcctgggtgct 720  
 ggacactjgg gtaagagttt ggaagctatt ggctgggcaa ggtggctcac gcctgtaatc 780  
 ctgacacttt gggaggtgta ggcaggtgga tcacgaggtc aggagattga gaccatcttg 840  
 gctaacacgg tgaaacaccg tctctactaa aaatacaaaa aaaaatttag ctgggcgttg 900  
 tggcatgcgc ctgtagtccc atctactcgn a 931

<210> 114  
 <211> 588  
 <212> DNA  
 <213> Homo sapiens

<400> 114  
 gattcggcac gagatcaaaa tggccagttc tgtgacagta aaagaggttt gtgtcttatt 60  
 taatcttttg ataataataa cagctatggt gtatcacagc tttaccaagt accagacact 120  
 gttctaaggc ctttgcatgg ttcactcact ccttacgtca tccctcggtg gcaggtgctg 180  
 taattatcct tatattgcag acaaggacat tgagacagag gtcaagccac cttccaagg 240  
 gcacacatgg catctgcact gctcctgacc gaccgacaga gagagctgct gtcacgatcc 300  
 tcaaatgagc tatgcatgtc aaaagttaa aaataaaaaa gataaaaaa tgcacaaaat 360  
 ttaaaaagta aaccatttca agctggacag actaaaactg agagatggcc agagaagagt 420  
 atgaaagata aatctatgga cagagtaaac cctgactggc ttgaaattag ggcccttact 480  
 cctccacact cctgacgggt tggttcaaga ccargaawta gaagcmcmmt gtgagttcta 540  
 cgstgctgcc ctgggaaaca cacaggctaa acacacccac aggctcga 588

<210> 115  
 <211> 812  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (443)

<223> n equals a,t,g, or c

<400> 115

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ctcttctgag gtcttctctg gagcagaaca gtacacatgg tctggaattg ggttgcacgg	120
aataactttc aaggaaagcc actgaataaa gtgccctgca ttcctgtcca ttggatactg	180
ataatgctat aagatgatct ttctcttctt tattttgttt gagattattg tgactctctg	240
gctaactcct acttatcctc aggccttttc tgaactcaca attcaaatta cagctccctt	300
tggttctctt ccacagcagt tgtacttaca tatgtctatt atataattat gaattgttct	360
atattgtcgc ccttacaggt aaactaatga atttggggct ccatctgttt gctcaccact	420
tgatcctggc agtagcacac aangggctgct caatacctat ttactgaatg agcaaakgga	480
ctggaccact tttagagact ggagtatctt cttawaccak gtgagattga wttttgagga	540
cagtttacca ctggaagctt ttgcagaact aaggtcattt ttacagtata cataacctct	600
gctgtgtttg ttgatactgt aagtttacct ttctttatga ctctttttaa gtagagcacc	660
cctgtgttta ggaaagctag agctattgtg atgcctttga gtttgcttgg ctgattgctg	720
ggacttgaac tactgagctt atctaaaagc ctcagaggcc ttgtagcctc tgtcttttag	780
agagtgtagg taaaggcttg ttttccctca aa	812

<210> 116

<211> 506

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (13)

<223> n equals a,t,g, or c

<400> 116

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cgcgttggcg gccgctctag aactagtggg tcccccgggc tgcaggaatt cggcacgagc	120
acctcctgag gaatatgggt taggaaagcc acccgctgct tttctggctg ggatggctct	180
cttccttggc tgctggaggg actggagaga ggtctgataa ggatggctgt atggatcagt	240
gggtcttatt cctcattctg cagcagaagc aactgggatg ttttttctcc taatattgtg	300
ctggcttctc tgcctttctc tttccggtct gtatccaagg ctgctaaacc ctggtggctg	360
gctctccctg ctctcttctc agatggatta tggctggatt ctgccatggg gagcttgtag	420
agtcagacat ggaaagccag gaatgggaaa gaggtcaggt ggttctctcc cacacctcac	480
tgcttgggtg ctatgtctca cctcga	506

<210> 117

<211> 751

<212> DNA

<213> Homo sapiens

<400> 117

gaattcggca cgagagcctc gcaggtggat tagaccaccc cgaggctcgg gagaaaccac	60
ggcaccttgt tgttttgagc cactaaatgg cgggacgctt gttcacgctg ctgctatggc	120
aagagctagc gaggcggctg gtaccgggtg atgcttcacc acggctttcc agaaagcgct	180
ccgtgacccc aggccacccc ttcccgacac tcacggttcc ctcagaaatg ctcctctcaa	240
atctctcact ctccctgcag cctttgttgt ttcttttttc tttctttctc ttttgcaaga	300
tgggatcaag gaaaggctc agacacaaaa cgcaacattt ttcttccatg acagatcaga	360
tattgaaggg ctcatgagg agccctgctc tgggacaact ccatgattag cgctccaaga	420
ggcagtcaca gggaagcagg tgctctgttc cctcctggc tcagcaatcc cgcagtccctc	480
ccgtcccgtc ccaggccag ccagcctggc tgcttggatc cgagacaata gcttggctctg	540
gaggcggctc aggggtggag ggaccacggg acccgggcac cagtacagca gctgggaatt	600
caggcccagg gatagggatg gggcacagga caccaccccc atctcacaca gggagatgaa	660
ggtgggatcc agcatgggga ctggacatcc ctgagtccag ctgccccgtt acaatggggg	720
aactgagatc cggggatggg atagttctcg a	751



<210> 118  
 <211> 960  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (460)  
 <223> n equals a,t,g, or c

<400> 118  
 ttttctctag tacatatatg taaatatatt aatgttggtt ttgtgtttgt gatgtagtaa 60  
 ggagatgtac atagaaattc attgaggtat atagatactc atctgtctag gcagttccca 120  
 attttctgaa gaatgtttta cagcaaaatt ttctattttc ttttattaaa tagtgacacg 180  
 tcaaacaatg tcacatccaa aacactagtt tcatcaattt ctgacagtaa taatagactt 240  
 gctgtaagta ttgttttctg atgccatacc cttgtcatac atattattaa atgaccaata 300  
 ttatgtatga agtagacaaa aaaatttact caaacttcat tcaaatccta attgtgataa 360  
 tttttgtttt atatttaatt ataaaccaa atacatttgc atttttaagc taatttgtct 420  
 caaaattttg ctttatattt ttggatcagg ttaaagtccn gtggatcccc tgaatgttat 480  
 tgtccctctt gatgggtttt acttctgagc tatacgtcaa aagacacata agcttcaaaa 540  
 gtcmagacaa acctcattgc cataaaaaatc aagatataga tgttctgttc cgtaaaactcc 600  
 ttgaaaaaca ttttaagtc atcaatatga tctgtttccc atgaaactta agttagcttt 660  
 cttattggag twatttctt tctgtaagtc tgaaaagtag agattttgtt ttacgcattt 720  
 tagtaacctg caacaaccaa ctctaaaaaa gatttggctt gtaatgacgg tctctgcttt 780  
 tttgggtttg gagtacacaa ttgtaattt tacttagtta ttgtgtttt tctttgttca 840  
 aggtattgac tagtttcata aattttttgm aagtttttct ttcattgggt ggaaagcaga 900  
 ttacattttg cactattaaa ataagtttat tacttttaaa aaaaaaaaaa aaactcga 960

<210> 119  
 <211> 1442  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (1377)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (1419)  
 <223> n equals a,t,g, or c

<400> 119  
 cttctatatt agatggacag atttatatac ttttccatgg aggattaagt aaactgaaac 60  
 ctaagacaca cgaagaaatt ctaagtggaa aggccactta ttagttagtt tacagcagta 120  
 tcgtaagtga caggatgata ggagtgtggt aagtgatcag gataataatc tgcttagtaa 180  
 gagaaacaat ttgaatttta gaaggaaatt gccttaccat ttgcaaatga aggttaattaa 240  
 aatacagtga atttcaaat gcctttttaa tgacaatgtg tgaacttaat ttgttttaatt 300  
 aaaccaaatt trttgttatt gtgttaaggc tattttacat tgaatgtgta tcttgccact 360  
 gatgttaact tatcccatct tacccaagggt tgtaggtaac aatatactat tgggtgacag 420  
 tggactaaca tctctagtga tccctttgtc agtgggtctt aacttaaaat aatttagaga 480  
 atatggtttc tacaacttac atttttgttt wcttgtaact acagattatt atgatggttg 540  
 taatgaagat tatgagtata attggagcta tatgtttctg aattctgaac aactatttat 600  
 aaaattttat cctacttttt tctgttgaac atatgacttc tctggtctgc taaacacata 660  
 cagaccttta gttttgtttt acatggattt aaatatatag atatatcact gtaaaaataa 720  
 cttcaggtgt aacagattta tagagaaagt aatcatattt gtttatggtt gtgtacctac 780

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tttgagaaga aaagaaaaat attagaatga acagataatt ttacaagtgt tgatcactta      840
ccagcaaacc agaaacttca gagattttga aagcaaatct attttctctg ctgtgtatta      900
aattcattta tctaaaatgt tattgtcctt ggcttagaat catcttgtgc aaattctctt      960
tttttgttgt ttgtctgttt gcctgttgct caccatagac ataattttct tttcataaaa     1020
cattctttgt ataatcacct cagagattat gaaagtgact ttgataaaat ttaatggtgt     1080
tcacaaaata attttcacgt gagtaatttc acagtgcgtg tattgtatgt tatttagtgt     1140
attttatatt ttgtttcaat tagagaatgc tattgaatcc agtttttgtt tagttactgt     1200
tcattttact ttataaaatt gacataattg agtttattaa atttattggg ccaattttaag     1260
taaacagttg aacgtttcat aagtcatgag gtcttttttg gcatatacat gaagtaacaa     1320
aagacaatac taggctatgt aataggragg ctaccttaat taggaggtaa atattcnttt     1380
tggaatttgg gcccggtggc ctcggttggg aaatggggna atatccctag gtaaaaaaat     1440
gg                                                                 1442

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<210> 120  
 <211> 845  
 <212> DNA  
 <213> Homo sapiens

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<400> 120
gattttacac agaacatatt ctctgcatga tttcagaaaa gaaaatctaa aaaggtaata      60
cgggtatttc aaataaaatc ctttctggta tgaaaggctc cattgatttt attaagcctt     120
cctttacctt gtagtacaag gtgctttaat gggatagaac taagcatatc aatatctata     180
actgcatttt gtgctagaca attactgttc ttttctctaa aatgtatatg tcaatttaca     240
aggccaggga tagaaaacac tccataattg ctttccttga ttttgctgag gatttggtat     300
gatttttagta agcaaaactgt tttttgggtt ttccttaatg tttttaattt tttttcctct     360
tgcaacaatg acggtgcatg ttcttataaa tataggaagg tccagatata aatagtaacc     420
taaagtctct gctgtgctta aaaaaaaaaa tcatgtggcc ctttcaatat ttgaactgct     480
aagcaatgac atctgtagtt ttatctcctt ttttatgtca tagaaattaa tatgatactt     540
taaatatgta aatataatac attaggtaat gctattattt atatctgtct taacataatt     600
taagttgtag ctgtgtcttg gaaatatttt taaggtaatc tatattcaca ttgcctgtgt     660
taatgctttt taaagtttgt atacatcaga tgtatatttt tggtttggca taagctacga     720
ttgtaatttt tcttggcttt ttgttcataa agaatttttt gaaggaatgg taacaaatgg     780
taatttaca atggtttgtg ataaacacat ttttacactt aaaggwaaaa aaaaaaaaaa     840
ctcga                                                                 845

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<210> 121  
 <211> 360  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (340)  
 <223> n equals a,t,g, or c

```

<400> 121
gaattcggca gagaatcagc atgtctatca cctcaaatac ttatttcttt ttattgggag      60
cattcaaaat cctctcttct agctatttga aaatacacac taaattactg ttaactatag     120
tccccctgca gtgctgcgga atgccacaac ttatccctcc tctccagctg tagtttagta     180
tccagtaaca tactcttttc atttcccttc tttgggcaga aggctagatg ttgcctgttt     240
ttgttttatt tttctgttcc acatatagcg cacgaaagca gagtgtattc aaaaaaggaa     300
atgtgtttga aaaaaaaaaa aaaaaaactc gagggggggg ccggtacceca attcgcccta     360

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<210> 122  
 <211> 944  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (932)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (942)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (944)  
 <223> n equals a,t,g, or c

<400> 122  
 tcgacccacg cgtccgcccc cgcgtccgga cagacccagc ctggagctgg ccctggcct 60  
 gtgtgctgac ttcttggggt cctcaaacca ctgtattttt ctggttgagcc tgtacttggg 120  
 gagagatcag tagcatttga ggaagtaaga gaaaagaatc atggtacctc agggtttctt 180  
 tccctttact cgctggcagc cattgtctgt gggcacctca tgtttttcca cactctactg 240  
 ggccgtggag gtaacgatca cccaggccag tctcctctgc ctgggatgag ccctctgaga 300  
 ggaggcctag cagggcaggc tccctctggg catccctgga tgcagcctct ggacacatgc 360  
 ctccctttaa gtgtccgggt gcagctcagg ttgagtggag gtagaaggag aaacagacat 420  
 gtttaccacg cgttttccaa agctcctgat ctttcccaag attgtaactg aaaactgctg 480  
 tctcttgttt tgttcgtttt ggggggtggtg gtgctggctg ggccatgctt gtgaagtgat 540  
 gtgtgtctct gatttaacgg attcactgtt ttctctgcta attgagagag cggtattttac 600  
 attattttatt tgttttgaca caagtgtttt cagtgtttta tcctagctaa tggcttctta 660  
 aaggtaataa aacccttcca acgtaattgg tcagataaaa ctttttttct tgtatgctta 720  
 aataaagcaa ttagtgaaag acttctatcc aaaatgactt ttttgcctt ttttaaaacc 780  
 aatttactgt tactggaac tttttgtaca ataawcaat caccgagatt aaagaaaaaa 840  
 aaaaaaaaaa aaaaaaaaaa aaggggcgcc gctctagagg atccaagctt acgtacgcgt 900  
 gcatgcgacg tcatagctct tctactacgt gnaccctaac tncn 944

<210> 123  
 <211> 914  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (909)  
 <223> n equals a,t,g, or c

<400> 123  
 ggcagagcaa gagatgactt tagatgagtg gaaaaatctt caagaacaga ccagaccaa 60  
 gcctgagttt aacatccgga aaccagaatc cactgttctt tccaaagccg tgggtattcg 120  
 agagtcaaaa tacagagatg atatggtaaa agatgactat gaggacgatt cccatgtttt 180  
 ccggaacccc gccaatgaca tcacatccca gctggagatt aatttttgga acctccctcg 240  
 tcctgggctg ggagccagag gaggcaccgg gggaggccgg ggaaggatca ggagggcaga 300  
 gaactatgga cccagagcag aagtgggtgat gcaagatgtt gccccaacc cagatgaccc 360  
 ggaagatttc cctgcgtgt cttgaaagag cctgtttcc cagcaccgag gagctgcact 420  
 gcacacctgt ggggagactt ttccagctgg gccaaaggag tcagactcta agaacaatag 480  
 atgttgcttt tcccgtgtca tgtaaatttg ttgactttt ttgggctgag ctgttagagg 540  
 ggcttctcca gaggctcgag agcaggccat ttccaagaa gatgaagaat ggtgactgtg 600  
 tttttattga aggaatttca aatgaagaat aatgttttaa atgtgtatat agagatagta 660  
 tagactctc cgcggaagca tggagggaaa ggaggttgta aaatagactc catggagact 720  
 cttaggaagc agtagattcc cgggggctgt gcctttagcg ttagaggaaa cacatagagc 780  
 tggaaactgtt aatggaaagc agtcacagct gagttttcgg agaccaagaa attaaaatac 840

aattgcactt acaaaaaaaaaa aaaaaaaaaa aaaaactcga gggggggccc gtaccaaatc 900  
gccttgnt gcat 914

<210> 124  
<211> 462  
<212> DNA  
<213> Homo sapiens

<400> 124  
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ctgcagctgt gagccaccat gccagcctt aacttggtt taagacctct gatttgcctt 120  
gcctcaatta cctcctttct tattttcttt cctttgttga ctctcatact ctgttctct 180  
aattctcccc cttttccact cctgcccac cctgaaagac acacacacac acaataagtg 240  
ggtggagtaa gaagtcaacg gagttggata taagcattcc tgcttttctg acatctccag 300  
tgtcttgag aacaaggatt ctagaatgag ggctcctcat tatgcttctt ttcaacattt 360  
tttctctgtg ttacttaagc tttcaccca agcatgtttg acagagagcc agtgcattcc 420  
ccttactttt tacaaaaata aaaaaaaaaa aaaaaaactc ga 462

<210> 125  
<211> 545  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (7)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (16)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (41)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (42)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (87)  
<223> n equals a,t,g, or c

<400> 125  
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acagctatga ccatgattac gccaaagmcga aattaaccct cactaaaggg aacaaaagct 120  
ggagctccac cgcggtggcg gccgctctag aactagtggga tccccgggc tgcaggaatt 180  
cggcacgaga ttcgctgcct aattccacca tgatgtttta ctatgcatgc tttatcttat 240  
actcatctct ctctcctctc tctctttctc tttctccctc cctcctttct ctattataat 300  
ttagtcatct tattttttga ggcatttcag aatatatcac acttgctcta aatacttcag 360  
tatgaacatc attaactaga atttattctt tgttttactt ctgatgtgaa ayytatataa 420  
atacaacatg ctatgaattt gttttccmaa aaaccaatca acaatttawt aagcatggka 480  
acaaaaaacc tgaaggcttt atctttttaga gtagtagttt ttaaaaaaaaa aaaaaaaac 540

tcgta

545

&lt;210&gt; 126

&lt;211&gt; 912

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (906)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 126

gaattcggca cagagaaaca tttcatcccc agtaagattc ctcacgtca ttcacaggtg	60
atctctgttc ccaccctagc cttggacaat tctgcaccta cttttagtct ctataaattt	120
gccttttctg gacatttcat gtaagtcgat cacacagtat gtgttccttt gtgactggct	180
gcttttgctt agcatgacgt tcttggggct cgcaacgcag cttgtgtctg ttgttcattc	240
cttttgcagc agaatcgtat tctgttgttt ggatgggcca cctgtttgtt gtctgtttac	300
tctccagctg gtggacattt aggccgtttg cactggcggt tactgtgaat catgtcgtg	360
tgaacattgt gtgtgtgtct gcgtggactt gtgtgtcctg ttctctggga aggagtgcg	420
ggtagargg tagttttttg ttccctctgg agactctctg gtttccacat atggtagttt	480
tatgcttaac cttttgagaa attgccaat ggctttctga agtggccacg tcattttgct	540
ccctccagcc gtttgtaatg ttcccatttc tcctatgtgt aattttaata caaagcagta	600
aaaagttgcc attatggacc tagtaaattc tgaggtaaca taagagagaa ataatgatgc	660
agccgtcatt actgtgctgg taatgtaagt ttcccttttt tttgttttta aatggagctt	720
tgcagagatc aagtcgagag aagaacactg ggccagcctg actccaaagc ctactctctt	780
aagcgctttg ctgacttgtg atgtttttaa atctagcatt attttcaaat gctgtgagag	840
cactgaagat aaaggatttg attctttttt tcaggcatcc aagatggtt catcatcaag	900
aatcanttta at	912

&lt;210&gt; 127

&lt;211&gt; 1048

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (13)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (16)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (17)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 127

gatcccccg gcncgnngaa ttccggcagc gggacagagt agttccagag gcagttctca	60
ctgtgacagc ccttcgccac aagaagatgg gcagatcatg tttgatgtgg aaatgcacac	120
cagcagggac catagctctc agtcagaaga agaagttgta gaaggagaga aggaagtcga	180
ggctttgaag aaaagtgcgg actgggtatc agactggctc agtagaccgc aaaacattcc	240
acccaaggag ttccacttca gacaccctaa acgttctgtg tctttaagca tgaggaaaag	300
tggagccatg aagaaagggg gtattttctc cgcagaattt ctgaaggtgt tcattccatc	360
tctcttcctt tctcatgttt tggctttggg gctaggcatc tatattggaa agcgactgag	420

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cacaccctct gccagcacct actgagggaa aggaaaagcc cctggaaatg cgtgtgacct 480
gtgaagtggg gtattgtcac agtagcttat ttgaacttga gaccattgta agcatgaccc 540
aacctaccac cctgttttta catatccaat tccagtaact ctcaaattca atattttatt 600
caaactctgt tgaggcattt tactaacctt ataccctttt tggcctgaag acattttaga 660
atttcctaac agagtttact gttgtttaga aatttgcaag ggcttctttt ccgcaaatgc 720
caccagcaga ttataatttt gtcagcaatg ctattatctc taattagtgc caccagacta 780
gacctgtatc attcatggta taaattttac tcttgcaaca taactaccat ctctctctta 840
aaacgaagtc aggtttagcaa atgatgtaaa agaagcttta ttgtctagtt gttttttttc 900
ccccaagaca aaggcaagtt tccctaagtt tgagttgata gttattaaaa agaaaacaaa 960
acaaaaaaaa aaggcaaggg acaacaaaaa aatatcctgg gcaataaaaa aaatatttta 1020
aaccacaaaa aaaaaaaaaa aaggggggt 1048

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&lt;210&gt; 128

&lt;211&gt; 722

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (251).

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 128

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gaattcggca cgaggaaagt ttcaaccctc tgacatgtgg gttcagctta tttttttctt 60
tggtcagtat ggagactctc ttacttctgc tttttttcct ttctcttcta atttttcgct 120
tcagaattct ggtttctcaa tgcataaact gaagtaattt ctccattctt acttttctct 180
gccccaggct tgagatagaa ctaggagagc cagtgaaggc ttttctttcc taaattaaca 240
ggcatctgtg ncataaatgc tacctttgaa ctatgtgatt taagataatg tgcagaagta 300
cttctctggt ctttcaggtt gcytgcataa ctawgtactt ggttgaactt gtaattcttg 360
ctgacaacag tctgtctggt ttccagtaag gttcgtgatc ctccgggcaa ttttgatcag 420
tccctacgtg tactgaaaca tgccaagaag gttcagcctg atgttatttc taaaacatct 480
ataatgttgg gtttaggcga gaatgatgag caagtatatg caacaatgaa aggtaaagaa 540
attgaaaaat gaaaaatctt tcccatgtaa tttgagtaat agccaggaac ccactcactt 600
tgaagggcct tctaagaaca aagaaaagta tatggttata gatggcagca tgaaaaggaa 660
accaacttgc acatgcaccc tcaaatctaa aatacaagtt aaaaaaaaaa aaaaaaactc 720
ga 722

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&lt;210&gt; 129

&lt;211&gt; 477

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 129

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gaattcggca cgagggtgagt atggcttttg tcttccatct tgctcagggt actttggaac 60
cgctatacat tgcaggagct tagcttctgg ttaccatggt ttgcttcag agcaacaagc 120
ctagtacttc aacatggaga caattatctt ttgtttttgt ttgtttttgt ttgtttttgt 180
ttggccatgc ctttttgagt ttaccttttt atattttgtc catcattgcc atgtgttttg 240
agcagtgggc gttccataac atgaactcac tgtaccatca cgaatgggaa gtaaggggaa 300
accttatcca tgtggatttt actcttccct gattccctaa attgggtttg caaaatacta 360
ctgtgcactt tcttgatgat tcgggcttat ctttatgact gtctgtkttt gtgtcagact 420
gtaaagaagt ataaagtctt ttagcttgaa aaaaaaaaaa aaaaaaaaaa aactcga 477

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&lt;210&gt; 130

&lt;211&gt; 1296

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 130

ggcagaggc	cactggaatc	tgatcctgat	tgtcttccac	tactaccagg	ccatcaccac	60
tccgcctggg	taccaccccc	agggcaggaa	tgatatcgcc	accgtctcca	tctgtragaa	120
gtgcatttac	cccaagccag	cccgaacaca	ccactgcagc	atctgcaaca	ggtgtgtgct	180
gaagatggat	caccactgcc	cctgggctaaa	caattgtgtg	ggccactata	accatcggtg	240
cttcttctct	ttctgctttt	tcatgactct	gggctgtgtc	tactgcagct	atggaagttg	300
ggaccttttc	cgggagggtt	atgctgccat	tgagaaaatg	aaacagctcg	acaagaacaa	360
actacagggc	gttgccaacc	agacttatca	ccagacccca	ccaccacct	tctcctttcg	420
agaaaggatg	actcacaaga	gtcttgtcta	cctctgggtc	ctgtgcagtt	ctgtggcact	480
tgccctgggt	gccctaactg	tatggcatgc	tgttctcatc	agtcgaggtg	agactagcat	540
cgaaggcgc	atcaacaaga	aggagagacg	tcggctacag	gccaagggca	gagtatttag	600
gaatccctac	aactacggct	gcttgacaa	ctggaaggta	ttcctgggtg	tggatacagg	660
aaggcactgg	cttactcggg	tgctcttacc	ttctagtcac	ttgccccatg	ggaatggaat	720
gagctgggag	ccccctccct	gggtgactgc	tcactcagcc	tctgtgatgg	cagtgtgagc	780
tggactgtgt	cagccacgac	tcgagcactc	attctgtctc	ctatgttatt	tcaagggcct	840
ccaagggcag	cttttctcag	aatccttgat	caaaaagagc	cagtgggcct	gccttagggt	900
accatgcagg	acaattcaag	gaccagcctt	tttaccactg	cagaagaaag	acacaatgtg	960
gagaaatctt	aggactgaca	tccctttact	caggcaaaca	gaagtccaa	ccccagacta	1020
ggggtcaggc	agctagctac	ctaccttgcc	cagtgtgtac	ccggacctcc	tccaggatac	1080
agcactggag	ttggccacca	cctcttctac	ttgctgtctg	aaaaaacacc	tgactagtac	1140
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cacttctcac	atgtgtctta	agggagcaca	aataaaggta	ttcgattttt	aaagataaaa	1260
aaaaaaaaa	aaaatttggg	ggggggggcc	ccgtta			1296

&lt;210&gt; 131

&lt;211&gt; 738

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 131

gaattcggca	cgagtgcaca	gaaagacggg	gtcagatgca	cattaatctt	tagcctgatg	60
tccttcatga	tgtccaacct	ccagtttcat	ctcctgccac	actcatcccc	catacttcca	120
ctcttcacac	tggccttact	caaaatgcag	attccaggac	tcaggctatc	tcactgcctt	180
cttacttaca	attctttatac	cagaacaccc	ttcctcctcc	cctcatctga	atcttacctg	240
gtttttgaaa	tttaagttag	ggccttctta	ggaagatttc	cctgattcag	atccaagttg	300
aattatgata	accctccttt	ggctcccata	aaatcttata	acttcttaac	tgtgttttat	360
gaatagttgt	ctagtcttagc	actatgtcag	gagctattga	cagcagggct	gggcacagtg	420
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ctcaagccca	tccagcctag	gcaacagaat	gagatcttgt	ctgtacaaaa	aaacaaaaga	540
ttaattgggc	gtggtgacgt	gcacctgtag	tcccaactac	ttgagaggct	gaggcaggag	600
gattgtctga	ccccaggaga	tcgaggctgc	agtgatccat	gatggtgtca	ctgcactcca	660
gtctgagcaa	cagagcaaga	ccccaccccc	caaaaaagct	attgagggtg	gcagtttact	720
ttcattgttc	tacctcga					738

&lt;210&gt; 132

&lt;211&gt; 442

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (306)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 132

gaattcggca	cgagtgcacc	agaagggtga	gtcagttggt	agtgtggggt	gcatgagggc	60
cattgcaggt	tttgataatt	accctttatt	ttaatttgat	catacttttt	tgtttataac	120
cttattctaa	aaataattca	aggtgaccat	gcttccatta	tacttcttgc	aaccatacct	180

atcttttggtg atatttatta tgttaagga caattggcat cttttggccc ttacctgtag	240
ctattctatc atctggagat tatctccaga cacaaatcca tcgcccattg ctccatcgag	300
gcacantcag ctckttgtag ttgccattgc ccctctcgag ccttctccac atagccacat	360
gcaatccatt cccaaaaacc tagctcaatt ttcctcatca cagatgtttt ccctgaccct	420
ccagttggta tatatctcct cc	442

&lt;210&gt; 133

&lt;211&gt; 882

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (881)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 133

gaattcggca cgagatgttt tcttcaactca aaaaatttta tattctcaaa catgtatatt	60
ctttccctgt cttgttccat ttcttttctt tttttctttt ttcttttctt ttcttttctt	120
gggctgagaa aggggcaggc aaaatgaagc tggccactga aaactgtaag atggtaaaaa	180
gctgacagcc tgtgtatgtg aaaagggaat tgtaaatgga ctgcaatgta atgtacactg	240
taatttgaat acaattactg tatctaaaag gagctgctat gaagtacctt tcttatgttg	300
ctaggctact gtttctgaaa gccctggatc tctttgcacc aaaaatggtc cagatagact	360
ctttttaagg atcttggtg ctttttacta gaaggttgct tttatgagca tttttatact	420
gctgaaggat gagtgtaaat tttaattaac tttgccgttt tgtagagaaa actattccac	480
aagataaatt ccaagtcttt tcacctgtca ggcatgcata ttttaatatc tgtttggata	540
gtcagaagta gaatcataaa ggtaaaatat gagttgttac tttgtttctt cgatgtcata	600
ttttatgtgt aatatatatg taaaggcca ttcttaagtt ctctccttaa acttaagtct	660
gtcaagtgtt agatgtgtgc atgtgaactt gttgcaactg agaaacatat tcagagttaa	720
tctatgtaac ttattcactc tgtaaataca tttaaagttt ttgtgatgta agcttaattg	780
atattctggt cagaacttty tttagwctaa araaagttct gaacagaata tcaattaagc	840
ttacattgat attctgttca gaactttctt tagctagaaa na	882

&lt;210&gt; 134

&lt;211&gt; 1032

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (5)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (593)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 134

ggcanaggga accaccttct gtagaacatt caaccaggcc cagatccaga aggcttgagg	60
ccctgtgggc cccatccttg gggagaagtc agctccagca ccmataagg gcacccctcg	120
tgctggatc actgcagtgc ttgttgacgc tgtagaatyt ytgcagctgc tgcaagttaa	180
ttcatgggaa aaatccctgt tcaacagcat tgcctctgaa tgccctcac atgccaacac	240
cagctgtatc agctccctcag ccagctcctc tctagagaca ccagtcagat tataccagaa	300
tatgttctgc tcagcggaga actgcagtga ggagacacac attacagcct tcaactgtcca	360
cgtgtctgct gaagaacact ttcatcttgc aagccagtgc tgccaaggaa aggaatgcag	420
caacaccagc gatgcccttg accctccccc tgaagaacgt gtccagcaac gcagagtgcc	480
ctgcttggtta tgaatctaata ggaactttcc tgtcatggga agccctggaa atgctatgaa	540



gaagaacagt	gtgtccttcy	tagttgcaga	acttaagaat	gacattgagt	ctnaagagtc	600
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aacaagactc	ttggaggagt	catctttcga	aagtttgagt	gtgcaaatgt	aaacagctta	720
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tgcccagcac	cccatttctg	cttctctgag	gtccagagca	tcccctgctg	tgctgacacc	900
ctctttccct	gctctgcccc	gtttaactgc	ccagtaagtg	ggagtcacag	gtctccaggc	960
aatgccgaca	gctgccttgt	tcttcattat	taaagcactg	gttcattcac	tgaaaaaaaa	1020
aaaaaaaaaa	aa					1032

&lt;210&gt; 135

&lt;211&gt; 1766

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 135

gtkattcaaa	gccatcacia	aacactataa	gactgaccaa	aatttagata	acctttgaac	60
cacgattttt	ttccacatct	gtctgtgaga	cacagcgcaa	tgtacttgcc	cttccagaaa	120
ctgtgctaaa	aagagaaagt	ccaaaagact	ctaaacaaaa	acctcgagcg	cgttgaggat	180
gtgtttcatt	ctgggtgtct	gttttgcaag	cttgataaca	gaatgtccgt	gccattgtaa	240
atgtttaga	gatgtgggccc	gtggcccaac	cgctctatat	gagatgtagc	atggtacaga	300
acaaactgct	tacacaggtc	tcactagtta	gaaacctgtg	ggccatggag	gtcagacatc	360
catcttgtcc	atctatagtc	aagaagtgtt	tccagatcct	ttggaaaggt	gggcatgggg	420
caggtgcttg	gagagtggcg	tttgagccag	agcgacccca	tttcccgtgt	gaaccatagg	480
cacaacccag	gaagtttccc	cacttgtagg	agtgtgggta	ttccagagca	agactgtggc	540
caccatcttc	ccctcttggt	gttttccgaa	agtgcacgtg	ttggatcatc	catgaccact	600
gaagcttagt	aaccagcgcc	aaaaagtaga	ttcatcaaac	tagagacccc	agctcccctt	660
ctcgccatct	tctttctcaa	gttgaccgtg	gtgctgtttc	tggaaggcat	ctgcaactcc	720
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caactcagag	gaacccttcc	tccagcgtct	ttggcatggt	ttctaggggtg	agagttccca	900
atttggatag	aacggccacc	atattgggta	ctgaatctct	ctcccctgtt	tttattacgt	960
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tcaaagatgt	agctagcatt	ttgaaaccat	atgggcaaaa	cccggcaacc	agaaggggac	1140
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ccaaacagtc	aacaaaacac	aaaccctgaa	ggaaaacctt	ttccatacac	ccagggtatg	1260
cattgaagag	ttttccactg	tatacathtt	tatccagatg	aaggtatttt	tatatattga	1320
caataggaaa	cagtgaccat	tttcagagta	atcaaactctg	gaacaaatga	aacatctttt	1380
agccaccacc	accctgttgc	aattaagaca	accgtggggg	aacacaccac	tttttactgt	1440
tgaaaccaac	acaacgttga	aatccaggct	tatacgaga	ctccgattcc	ctagagaact	1500
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ttgtttaaaa	ttttaaaaaa	aggaacacgt	tctgtaaacg	agtcgctaaa	tacagaattg	1740
tataataaaa	aaaaaaaaaa	aaaawt				1766

&lt;210&gt; 136

&lt;211&gt; 470

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (315)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 136

ccgccgccgc	cgctacagcg	accctgaccg	ccgtccgagc	cgccagacac	ccagagagac	60
gccagaggcc	gcggaggggc	gaagaccggg	agtaactctc	ccttccaccc	caacccgat	120
cgccagccct	cgagagctct	gtgctccacg	ccgaggatgc	accgtctctg	gattgggtccg	180
gccttcttcc	taatgacatc	gctcagcgtc	tctggagccg	tcattcccgcg	gaatgggggc	240
ccaggggggtg	tcagytccgg	gccttgcttc	ttgcagctac	tctgtgtgca	ggccgggtcc	300
tccaccatca	ggaanatccc	atcctgagct	ctgtctctctg	ccccctctgc	tgtgggatgc	360
tgagcacaga	gcccacagcc	catctgcctc	ttcacctccc	tgaatccgtg	tccatctgca	420
ataaacgaca	gcctcggtcg	cctcgtgctg	aaaaaaaaaa	aaaaaaaaaa		470

&lt;210&gt; 137

&lt;211&gt; 1168

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1163)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 137

ctggatctat	agactcttct	tgccctaaag	aatggcatgt	ttgcactcct	tcccccaaca	60
tgtacagatg	cctgtcactc	ttgggtgactt	tgtctgggctt	ctagtccctg	cagatgttta	120
aggagcaat	gaatggggag	tgtggatgca	aactacggcc	tccttggcac	tgtttcagat	180
gggggatttc	ccttctctag	gagaacctgt	gctggaaaag	gtgtggcacc	cacactgaaa	240
tggggcaagc	tcttcccagc	tttgtggggg	cccttggaaa	acatccactg	agatggaggc	300
agtcttcttc	ctcttcttcc	tcctgctcct	cttgacctgg	accagcaaga	tagcaccaat	360
ccttttctcc	tgatggcagt	atctgaatga	ctttcacagc	tgaaggccag	agaccagcct	420
agctggga	ttcaggcttc	aaagctttgg	tgaggatgac	tccagaacca	ggcaggtagt	480
ccccctccag	gatgccatgg	cctaaagcat	ttcactcctc	agtcactagg	ctgtgaactc	540
attgtggctg	acacttttat	tcgctgctat	gttttttagc	aatgcccggc	acacagacct	600
gcttactatg	cttttgctga	gtgagtgaag	ggataagtcc	ctttctgcct	ttttgatact	660
cactttgggtg	ccccctgagg	tcacagagac	ctggatttga	cttctggctc	tgccacacaa	720
gagcacggat	gctttgggtc	agttacttca	gctctgagag	gctcaattgc	ctcacctgtg	780
aaatgggtta	gtgattccag	gaatcttacc	aggcccatg	gacagcatgt	acataaagag	840
cctagccctt	ccctctcctc	cctctccagg	ggccaggcct	gactcccctg	aagccatttc	900
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ggaacagggt	ctaagattat	gtagatatag	cacaaagcct	tgctcctgct	cgtgccgaat	1140
tcgatatcaa	gcttatcgat	acngtcga				1168

&lt;210&gt; 138

&lt;211&gt; 1294

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 138

gatcttgtcc	aagcagtcgg	ggctacttcc	aagaatgtca	gctcctgtta	gcaaccagtg	60
gagtcctggc	ttgggtctta	agttgacctc	tctatagctc	caaatcttac	caatctcaga	120
aaactgtgaag	aggcacagat	gactccacca	gctgcagagt	gactctgaag	agagtcttca	180
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actgctgttg	ctgtctttcc	ccagctctga	actagtctta	aggtagctta	ggatgaaaaa	360
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aacctctctca	tttactctgt	ggcmwcaaaa	atccacaaaa	gatggattaa	ttgcactctg	780
gttaaatgca	gcagcacaat	gattaaaaatc	tatatctcta	tcttctctag	caccttggtg	840
tggggatggg	gcggaagggt	gtcttgaggg	gcagggagga	ccccataaaa	caatccctcc	900
tgcattctca	ggctaaatag	ggcccccagt	gactacctgt	tcttggtgtg	cccctctgaa	960
gagctctgcc	ttctcacagc	caccaccagt	tgccccactc	ccaggaaaac	agcacatgtt	1020
cttcttctcc	tgcttgaga	ctgcgtgtta	gtcttccatt	cataactcat	cagcagctca	1080
gtccttctta	tgtctagtct	cagttcatc	agccaaagct	catttttgtc	ctatccaaag	1140
tagaaagggt	tcttttagaa	aacttgaaga	atgtgcctcc	tcttagcatc	tgtttctgac	1200
tcccagttat	ttttaaaata	aatgatgaat	aaaatgcctg	ccctgaaggg	ttctggagga	1260
aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaact	cgta			1294

&lt;210&gt; 139

&lt;211&gt; 1720

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 139

aaccagaaagt	ggacgtgcat	gacagtggac	ctagaggctg	acaaacagga	ctacccgcag	60
ccctcgggacc	tgteccacct	tgtaaacgag	accaaattca	gttcaccac	tgaggagtgtg	120
gattacagaa	actcctatga	aattgaatat	atggagaaaa	ttggctcctc	cttacctcag	180
gacgacgatg	ccccgaagaa	gcaggccttg	taccttatgt	ttgacacttc	tcaggagagc	240
cctgtcaagt	catctcccgt	ccgcatgtca	gagtccccga	cgccgtgttc	agggccaagt	300
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ggactggccc	ctacccaaga	gtcacacttg	caggtgccag	agaaatcctc	ccagaaggag	420
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ccaacagacg	tctccatctc	caaaacagcc	ttgtwtccc	gcacaggac	cactgagggtg	540
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cagagcagag	atcataacca	aggasagaga	ggtctcagaa	tggaaagata	aatatgaaga	660
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agggtgtgaa	gagatgtgcg	caggagtacc	tgccccgggt	gaagaaggag	gagcagaggt	960
accaggccct	gaagggtgcac	gcggaggaga	aactggacag	ggccaatgct	gagattgtc	1020
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tgttttggac	ttactgtgtg	cgtgcaatat	gaccgtcggc	acactgctgt	tcctccagtt	1260
ccatggacag	gttctgtttt	cacttttttg	tatgcactac	tgtatttctt	ttctaaataa	1320
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attttcctag	tataattcat	agcaagtga	cctcagagtt	cctgtatcag	ggagattgtc	1440
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ttaaggagtg	taaacttgat	ctgcatttgc	tgatttggtt	ttaaaaaac	aagaatgca	1620
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aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaattc			1720

&lt;210&gt; 140

&lt;211&gt; 774

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (697)

&lt;223&gt; n equals a,t,g, or c

<220>  
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<222> (709)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (716)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (733)  
<223> n equals a,t,g, or c

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aatgttggat gaatgaatga agttgaagag agggtaggcg gggaacgagg atgaggggga 180  
cggctggaga agaggtatgg gaggttcgat gtttcaggga tggcacccaa ggggggacat 240  
tcgaggcagc accggtagca ctccctttgc gatgaggggc gtctctttgg acttcttgga 300  
aaagaggtgg gcattggaaa ccagggtctg ggaacaaacc gtggtttggga cataacattt 360  
gttaccttca cttttctggg agttggagaa gtagaggagg aagttcagac aatttcataa 420  
gtgtctaaaa agagacagtt atgcgaccat tgacgaggag taaaagtcgt ctattgagca 480  
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ctgtcagcct caaaggtctg aaccctagta tagattcttg tagcttgctt gaagttacag 660  
tgggtcatga tcaggaattg atgctttgtt tttgttntga aacggagtnt cgccantgca 720  
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<210> 141  
<211> 1566  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (415)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (718)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1116)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1122)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1127)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1312)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1373)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1455)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1456)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (1540)  
<223> n equals a,t,g, or c

<400> 141  
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tgtggtaaaa gagacataat gtctcggaga gagaacaaat ttctgcttta ggagtgttct 120  
tagttaaggt aacattagct tctataatac gcacactccc aaatctcagt atttcaacat 180  
gagtttctct cttgctcatg taaagactgg tcagggaccc aggttgacag aggtcttca 240  
gtacatagct tccaagattg ctgtgggtgt gacatccagc cagaaatctg gtgaagagag 300  
agcaatgatt acacaggaac ttttaatgga ccaggcctgg gacagcgtat gtcacttcca 360  
ccaacatccc actcaccaga atttggtcac agggccatag ctatctgcag agaangctgg 420  
gaaatggaac ttgctatgt gctcaagagg aaaagtaaaa cagttattga ataattagta 480  
ataattagca agtaactacc taggggtcac agaggacctc tcaggtagaa tttagactta 540  
aagatgatgg gggagtgtgt ggaagatggg tgcagaatag ggaaggggg gattgaagga 600  
agaacaagct ctgacttcac ctgcatgggt agagcccaca gtgttggtag ggacatgtta 660  
gctttcaaca tcagcttctt aacagtatta ttctttcatc ggaggaaatt agtctatntc 720  
tgaggaaaaa aaaatctgca atacgtagca atttacttac ttggatattg aatgttaaag 780  
cagagagaga ctttgtctc aaaaccctcc catttcagaa gtgaggagcc tggggagggtc 840  
atgctctctg gatgtcacac agtgagtcac tgcacaaagc agaatagaac ccagacctct 900  
cagtttccca ttccagtgtc ctttctatga ggaagata agtttgagca tttttaaac 960  
ttaattatgt agaaataacc atgatatttt atcgtaaatt atttcagtca tctcatttta 1020  
aattttactc caaactaaag gaaaacggta ctgattttaa acatctatca taattcaata 1080  
tagcccatat ttcttcttta ggaaaaattt ttttngttt tntatcntga agaccggtgc 1140  
cctcttctctg tgtctcatgt agacatttca cagtcctaat atacagagca agaatagatg 1200  
aaatcaacat gtttaccatt attctatcta aattttcaaa gaaaaagggg acaaaagggtg 1260  
agtgatgact gagttgcatg gctataattg agtttttgtt gcttttattt tnataatatt 1320  
ttaattgaca tagatgttta aatgtatatc aaaatgcatg tcacagctct tgnacaaaga 1380  
taaatttgac tctagagcac attttcttta gtgagaatga taaattatct cagagcttgt 1440  
gattctctac ttttnnaaat cataaggta gttctttaat taaaagataa agaaaagtag 1500  
gcattgtcca tgtagtgaag tcacttttat caggataatn tagtaaccaa aaaaaaaaaa 1560  
aaaaaa 1566

<210> 142  
<211> 1384  
<212> DNA  
<213> Homo sapiens

&lt;400&gt; 142

tcgacccacg	cgtccggccg	gactaaccag	ctcctccagg	cgctgggggc	gggtgtggca	60
ggaggaagcc	cgatcagccc	caggctgtgg	atgtgggaga	agggcgagct	cagggggcca	120
tcattggggt	ccccagagg	caacctggcc	tatcagggt	gctcctcctc	gtgtgggcac	180
tggcctggcc	cctgccttgt	atgagcttgg	agctgatccc	ctacacacca	cagataaacg	240
cttgggacct	agaagggaa	gtcacagcca	ccacgttctc	cctggagcag	cctcgctgtg	300
tcctggacgg	gcttgmccg	gttgccagca	ccatctggct	ggtggtggcc	ttcagcaacg	360
cctccagaga	cttccagaac	ccacagacgc	gagctgagat	cccagccttc	ccacggctgc	420
tgacggaggg	gcactatatg	acactgcccc	tgtccctgga	ccagctgccc	tgtcaggacc	480
ccgcaggcgg	cggcagggac	gtccccctgc	tgccgggtggg	caatgacccc	ggctgccttg	540
ctgacctcct	ccagccgccc	tactgcaaca	gccccctccc	cagccccgga	ccttacaggg	600
tgaagttcct	cctgatggac	gccaggggct	caccccaggc	cgagaccagg	tggtccgacc	660
ccatcgctct	tcaccaagg	aagtcgccag	cctccatcga	cacgtggcca	ggcgamgca	720
gtggtggtat	gatcgatc	acctctatcc	tctcctcctc	ggccagcctc	ctgctcctgg	780
ccttctggc	agcgtccacc	scacgcttct	ccagcctgtg	gtggccggag	gargccccg	840
agcagctgag	aattggctcc	ttcatgggga	agcgtacat	gacccaccac	atcccaccca	900
gcgaagccgc	cacctgccc	gtgggctgtg	agcctggcyt	ggaccccytc	cccagcctca	960
gcccctagcc	tggcccttgt	ggctggggcg	tgtgtggctg	tggccagtgt	gggggcaagg	1020
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tgtaggacag	atgtcagggt	tctagacgtc	tttgggtcaa	aaagggggtt	ttattcaagc	1140
acagggacag	gacccatggg	cagggagagc	ggcaccgggg	tggtagagg	tggcccggtta	1200
tatatacttt	cgagtgggga	gggcttagag	agagcgtaag	tctctaagga	attttggaag	1260
caaggtctcc	agggtcctga	gggggctagc	tgttgtagg	aaaaggtcat	ttattactgt	1320
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ggcc						1384

&lt;210&gt; 143

&lt;211&gt; 537

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (429)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (502)

&lt;223&gt; n equals a,t,g, or c

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (520)

&lt;223&gt; n equals a,t,g, or c

&lt;400&gt; 143

gcccccaaaa	aagaaaggta	attaattata	gttcatttcg	ttttaactaa	gagttactaa	60
agcatccctg	gatgctgaga	ggtactctct	aggaggcaga	aacaggacca	agcactgccc	120
acttatctcc	acactatgct	accaattcac	ctgcagtggg	catgtgcttt	caggagtttt	180
ttgcttggtg	tagacagttc	tatgttcgtc	ttgtttcagc	accctcgttt	gaaggacaca	240
aagagctcta	gggtcataga	accaactctc	actaactgac	acagatatca	ggatccaacc	300
catgcccaca	gtattacccc	aagtctctaa	ctagctgggtg	taaccaataa	tggaaagaaa	360
aaaagtaata	ttctgttctt	caacttcaac	agagaataat	agtgaagaa	tggtgatatt	420
tttcctaana	tggactaaca	agtatcctga	gttgggaggt	gacttccaat	agtaaacaa	480
aaaataactg	agaaaatgga	gngaggaggg	aggggagagn	gagagtgggc	acagaag	537

<210> 144  
 <211> 680  
 <212> DNA  
 <213> Homo sapiens

<400> 144  
 aattttttgt atttttttagt agagacaggg ttccaccatg ttagccagga tggctctgat 60  
 ctcttgacct cgtgatccac ctgccttggg ctcccaaagt gctgggatta caggcgtgag 120  
 cmaccacacc cggccaatca tattttttct tgttactaat tagaatcatg attctcctgg 180  
 cattcttcat ttgtttatac ctcaattcct ttcccttagc aagatctttg ccatagagta 240  
 tggaaaccag gttccttgcc agttaatctg tattgtgctt tgtcatgtat tgttactaaa 300  
 cagctcaaga tcaaggggaa gaaatgtata tgaggctcag ttcattgttca gttttttttt 360  
 ttccagcatt gcaacattgc cactcatcat catgagtgtg gccctgtgtc aggtactgaa 420  
 ggtaaatggaa aaggtatata aggttgatcc ctgtactctt gttgggaact tgagtggat 480  
 gaatagagaa ggtgagttct tggggacaga ggctacagtt tagcaagctt tcctatgcgg 540  
 accttggtaa ttcttttaca ttttatagac caaagaacaa tcttaacttg cccttttttc 600  
 taaaggcatt gtttaaaaaac tgtcatcaaa tcattgcagt ttatggcaaa tggccttttt 660  
 ttaaaaaaaaa aaaaaaaaaa 680

<210> 145  
 <211> 1048  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (79)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (117)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (138)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (144)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (147)  
 <223> n equals a,t,g, or c

<220>  
 <221> misc feature  
 <222> (625)  
 <223> n equals a,t,g, or c

<400> 145  
 ggcacgagag aaagtgggcc cttaccaggc accaaatctg ccagcactct gatcttggac 60  
 ttccagcctc ctgaactgnt gctgcattc aaaagaacat tctattaaag ctacctnaat 120  
 ttggcgctta tttttctnaa tcangtnctt gacaatcata ttgtgtggaa tggttgctgc 180  
 tttaagtgcata ataagagcta actgcatca agagccatca gtatgttctt caagctgcat 240

gcccagaaag	ctggattggt	tttcaaagaa	agtgtttcta	tttttctgat	gacaccaaga	300
actggacatc	aagtcagagg	ttttgtgact	cacaagatgc	tgatcttgct	caggttgaaa	360
gcttccagga	actggaaga	aaatagttct	ggccagaatc	aaagattcag	ccctacaagg	420
atatgttttc	ctgtgaaatt	atctaagaga	atttcctgtt	gagatataaa	ggcccatctg	480
atcactggat	tgggctgagc	agagaacaag	gcccaacctg	gaaatggata	aatggtactg	540
aatggacaag	acagtttagc	atgaaagaag	atgggtgcaa	cttgatgttt	gcaaaagttt	600
cacaagttcc	tcgaatgaat	ccaanactgt	catgggtctt	actctgttac	ccaggctgga	660
gtgcagtart	taccatcggt	gctcactgca	gccttgactt	ccttggtccc	aagtgagcct	720
cccatctcag	gctcctgagt	agctgggact	acagggtttc	tatcctggga	gcaggagagt	780
gtgcctatct	gaatgacaaa	ggtgccagta	gtgccaggca	ctacacagag	aggaagtgga	840
tttgttccaa	atcagatata	catgtctaga	tggtacagca	aagccccaac	taatctttag	900
aagcatattg	gaactgataa	ctccatttta	aaatgagcaa	agaatttatt	tcttatacca	960
acaggatatat	gaaaatatgc	tcaatatcac	taataactgg	gaaaatacaa	atcaaaatca	1020
tagtaaaata	aaaaaaaaaa	aaaaaaaa				1048

&lt;210&gt; 146

&lt;211&gt; 930

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 146

tcgagttttt	tttttttttt	ttttggatat	ggagtctcac	tctgttgccc	aggctggagt	60
gctgtggtac	gatttcagct	caatgcaagc	tctgcctcct	gggtttaagc	aattctcctg	120
cctcagcctc	cccagtaggt	gggactacgg	gtgtgcaaca	caacatccgg	ctaatttttg	180
tatttttctg	agagacaggg	tttcacatgt	tggccaggct	ggtcttaaac	tcctgacctc	240
agttgatcca	cctgcctggg	cctcccaaag	tgctgggatt	acaggcaaaa	gccactgtgc	300
ccagctgcat	tgttgctgtt	ttttattggt	agttaagaga	gaccaaccat	tagaaaaatg	360
tttaaggctt	ttcaaaggaa	gaatcctatg	taggcagccc	cactacaggt	tacttttctga	420
tgaatgtcca	ggactattac	aaaatccatg	attgtggaaa	ttctgtcaaa	agagatgaca	480
gagaaatcct	gcctttggtc	acaatcctgt	ctgaccccaa	caaaagctaa	ggaatccta	540
atcagggtgtg	actcatgata	aagaaaaaca	tgcatccaaa	ttttggttca	gaagtacaga	600
aagtgtgcaa	cttctgtcaa	gttaattaat	gtatttgctc	cataactccc	cgacatataa	660
ggtaagtgtg	ttggagtatg	tgggttgaa	gctgctttca	aagatttaac	gtctttgatt	720
tttttagtca	ccatgggtgc	caggatagaa	taagatctgg	agactttcga	ataactgctt	780
acagatgtag	ataattataa	attgatacta	ataaagaatg	aagatctcag	cattccccag	840
agagggtctat	ttttagaaaa	aggaaatagc	caaaaacaaa	gtaaaacaaa	aaacatcatg	900
ggatatcagg	acttagctcg	tgccgaattc				930

&lt;210&gt; 147

&lt;211&gt; 830

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 147

ggtcgacca	cgcgtccgct	gaaaggaaaa	gcactgtttg	gagaatgac	cacctttcaa	60
gattttactt	attgttgata	atgctccac	atgtcctctt	ttttacgggt	gatcttcatt	120
cctaatatca	aagtgatatt	tcttctcca	ggcaccacct	ctttgatcca	cacaatggat	180
caaggagtta	tagcagcttt	taagtcttac	tacctgagaa	gggaggactt	tgcccagtc	240
ccatactgca	gtggaggaag	acactgagaa	gactctgatg	aaattctgaa	cagcatcaag	300
aaccttggtt	aggcttggtg	tatgtcgcta	aggactgtag	gaatggcacc	tggaagaaga	360
cacgcaagag	gtttgtcaat	aacttcaaag	gatttgccaa	ggatgaggaa	gttgcaaaaa	420
tcaagaaggc	tgtggttgag	atggcaaa	actttaacct	gggtgtggat	gtggatgaca	480
ttgagtaatt	cctagagggg	gttcctgagg	aattgactaa	tgggttgctg	ttggaactgg	540
aataggagtg	catagctgaa	gaagaggtaa	agaaaaagaa	agtcaggag	aagggaaaaa	600
agaactccca	agaatactca	cagtgatggg	tttagcagaa	gcttcctcag	actccaacaa	660
gctccttaag	aagtctgaaa	acatggaccc	caaaactgaa	aggtttttcac	taatagagag	720
gaaagttcat	ggtgcattat	ctgcctacaa	gcaaaaccag	gattcaaaaa	accctttgag	780
ctggagcttc	aaagcacaaa	aaaaaaaaaa	aaaaaaaaaa	aagggcggcc		830



<210> 148  
<211> 865  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (321)  
<223> n equals a,t,g, or c

<220>  
<221> misc feature  
<222> (409)  
<223> n equals a,t,g, or c

<400> 148  
ggtcgaccca cgcgtccgga gtagcagaaa ttgtcttctt tacaagtagt ctatgagagt 60  
agatgctgat ttctctaaatg taagggaata agaaaaactt catgattaac ttttttcacg 120  
tgtatttggg ctttgggtggg agtaggcaag aagaatatcc gtggatttat agagtaagca 180  
aaagtatgtc aggaaaaact aggaagaata gggctgaact gtggcttgat ttcaggagag 240  
tttctgggat tcagacttga attaaactgaa tgatgctgta atgtataagt gttggtatag 300  
gtgattttat gcaaagaaga ntaaacattg gcttactttt attatcgtat acgggatggg 360  
tgactactgc tgctagtcca aggtctkgat tttttaaaaa tgtgtttcnt gactgtggta 420  
gctgggagcc ccaggataca gacttttggg taaataacat ctgctccact ctgcttcccc 480  
gtgtgggccc ctctaaccct gggccaagca gttgagtctc tcctcggggg gcctggagtg 540  
agggtggata cagcttgggt aattcagcat ctgtacctaa aaacttactc aaagtaggct 600  
tcatgtaaag aagtcagtgg ttcttgggaa caggggtgag tgaatggagg cgaaggtgg 660  
ggccctccac aggtcagtca ggccctcagg gtgggacaag agctgtaggg ctcttggtta 720  
taaacctgtg tgggtggagac cagcagggtg gccaaactct tctttattat cagaacattt 780  
cactaataag ggaatccaag ggtcatctgg catcagcact ttaaccaata aaaaaaaaaa 840  
aaaaaaaaa aaaaaaggg cgccc 865

<210> 149  
<211> 545  
<212> DNA  
<213> Homo sapiens

<400> 149  
agccagggtt ctagtcatth aagatgyacc tgaataaaac aaagagcctt actctcctag 60  
aacttggtgt tctacctggg gagactgtca gtaaaccatc caaaaataa atacagcaga 120  
tgctgttaga agatgatggt gctatggtgt gctgtggaaa atagagaaag tagagggag 180  
tgagagggat tgcgtacact aggattgtga ctttacacag aagggtcagt ggtgccattt 240  
tagcaaagat ctgagagagg taaaggaata agctttgcag aagtgtggga gacaaatgtt 300  
ccaggtagag gaaatgacca acgccaagac cctaggggtg caatgtgtct gcttkgagtt 360  
ctagagaarg ggtatattat acatcgcttt ttgtgactca ctttttggca aacattatgc 420  
tctaaatga acctgtatth tgggaatawat ckgtggttca ttaattctca tctttgtaca 480  
gtattctatt atataaatac accatgattt atttagtcaa ttaaaaaaaa aaaaaaaaaa 540  
ctcga 545

<210> 150  
<211> 54  
<212> PRT  
<213> Homo sapiens

<220>  
<221> misc feature

<222> (54)

<223> Xaa equals stop translation

<400> 150

Met Gln Leu Leu Cys Ser Pro Tyr Pro Glu Glu Lys Pro Lys Gly Ser  
1 5 10 15

Asn Arg Asn Phe Cys Asn Trp Phe Leu Ser Glu Arg Ser Ser Cys Leu  
20 25 30

Gln Met Leu Leu Lys Gly His Lys Lys Leu Glu Leu Glu Lys Ile Asp  
35 40 45

Glu Ser Ala Gly Val Xaa  
50

<210> 151

<211> 46

<212> PRT

<213> Homo sapiens

<220>

<221> misc feature

<222> (46)

<223> Xaa equals stop translation

<400> 151

Met Ser Asn Leu Met Val Ala Met Ile Ala Val Ile Thr Ile Ala Val  
1 5 10 15

Ser Ile Pro Ser Thr Arg Ala Asp Thr Glu Ile Ser Tyr Thr Tyr Trp  
20 25 30

Ala Tyr Leu Ser Ile Leu Ala Gly Asn Asn Ala Trp Ile Xaa  
35 40 45

<210> 152

<211> 25

<212> PRT

<213> Homo sapiens

<220>

<221> misc feature

<222> (25)

<223> Xaa equals stop translation

<400> 152

Met Ile Met Glu Glu Ile Phe Leu Asn Leu Ile Lys Asn Ile Tyr Lys  
1 5 10 15

Ser Pro Tyr Ser Gln Cys Asn Thr Xaa  
20 25

<210> 153

<211> 265

<212> PRT

<213> Homo sapiens

<220>  
<221> misc feature  
<222> (71)  
<223> Xaa equals any one of the naturally occurring L-amino acids

<220>  
<221> misc feature  
<222> (80)  
<223> Xaa equals any one of the naturally occurring L-amino acids

<220>  
<221> misc feature  
<222> (86)  
<223> Xaa equals any one of the naturally occurring L-amino acids

<220>  
<221> misc feature  
<222> (93)  
<223> Xaa equals any one of the naturally occurring L-amino acids

<220>  
<221> misc feature  
<222> (95)  
<223> Xaa equals any one of the naturally occurring L-amino acids

<220>  
<221> misc feature  
<222> (133)  
<223> Xaa equals any one of the naturally occurring L-amino acids

<220>  
<221> misc feature  
<222> (157)  
<223> Xaa equals any one of the naturally occurring L-amino acids

<220>  
<221> misc feature  
<222> (183)  
<223> Xaa equals any one of the naturally occurring L-amino acids

<220>  
<221> misc feature  
<222> (204)  
<223> Xaa equals any one of the naturally occurring L-amino acids

<220>  
<221> misc feature  
<222> (265)  
<223> Xaa equals stop translation

<400> 153  
Met Ala Thr Pro Leu Pro Pro Pro Ser Pro Arg His Leu Arg Leu Leu  
1 5 10 15  
Arg Leu Leu Leu Ser Gly Leu Val Leu Gly Ala Ala Leu Arg Gly Ala  
20 25 30  
Ala Ala Gly His Pro Glu Cys Cys Arg Leu Ser Arg Glu Pro Gly Leu  
35 40 45

Cys Pro Glu Glu Ala Gly Lys Cys Pro Pro Gly Ala His Ala Cys Gly  
 50 55 60  
 Pro Ala Phe Ser Pro Ser Xaa Arg Asn Ser Lys Gly Leu Phe Cys Xaa  
 65 70 75 80  
 Asp Ala Pro Gly Phe Xaa Arg Gly Pro Gly Pro Thr Xaa Thr Xaa Asn  
 85 90 95  
 Glu Ile Asp Ser Trp Pro Lys Gly Ala Cys Pro Glu Arg Asn Leu Asp  
 100 105 110  
 Ile Asn Ser Ala Leu Thr Gln Gly Arg Thr Ala Val Pro Gly Ala Cys  
 115 120 125  
 His Leu Gly Ile Xaa Gly Thr Gly Ala Gly Ala Gly Ala Gly Leu Pro  
 130 135 140  
 Phe His Ser Arg Asn Pro His Ala His Ala Pro His Xaa Pro Trp Val  
 145 150 155 160  
 Thr Pro Val Ser Ser Asp Pro Val His Met Ser Pro Leu Glu Pro Arg  
 165 170 175  
 Gly Gly Gln Gly Asp Gly Xaa Ala Leu Val Leu Ile Leu Ala Phe Cys  
 180 185 190  
 Val Ala Gly Ala Ala Ala Leu Ser Val Ala Ser Xaa Cys Trp Cys Arg  
 195 200 205  
 Leu Gln Arg Glu Ile Arg Leu Thr Gln Lys Ala Glu Tyr Ala Thr Ala  
 210 215 220  
 Lys Ala Leu Ala Thr Pro Ala Ala Thr Pro Asp Leu Ala Trp Gly Pro  
 225 230 235 240  
 Ala Pro Gly Thr Glu Arg Gly Asp Val Pro Leu Pro Ala Pro Thr Ala  
 245 250 255  
 Thr Asp Val Val Pro Gly Ala Ala Xaa  
 260 265

&lt;210&gt; 154

&lt;211&gt; 237

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (137)

&lt;223&gt; Xaa equals any one of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (151)

&lt;223&gt; Xaa equals any one of the naturally occurring L-amino acids

&lt;400&gt; 154

85

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Met Lys Gly Ile Leu Val Ala Gly Ile Thr Ala Val Leu Val Ala Ala
 1             5             10             15

Val Glu Ser Leu Ser Cys Val Gln Cys Asn Ser Trp Glu Lys Ser Cys
      20             25             30

Val Asn Ser Ile Ala Ser Glu Cys Pro Ser His Ala Asn Thr Ser Cys
      35             40             45

Ile Ser Ser Ser Ala Ser Ser Ser Leu Glu Thr Pro Val Arg Leu Tyr
      50             55             60

Gln Asn Met Phe Cys Ser Ala Glu Asn Cys Ser Glu Glu Thr His Ile
      65             70             75             80

Thr Ala Phe Thr Val His Val Ser Ala Glu Glu His Phe His Phe Val
      85             90             95

Ser Gln Cys Cys Gln Gly Lys Glu Cys Ser Asn Thr Ser Asp Ala Leu
      100             105             110

Asp Pro Pro Leu Lys Asn Val Ser Ser Asn Ala Glu Cys Pro Ala Cys
      115             120             125

Tyr Glu Ser Asn Gly Thr Ser Cys Xaa Gly Lys Pro Trp Lys Cys Tyr
      130             135             140

Glu Glu Glu Gln Cys Val Xaa Leu Val Ala Glu Leu Lys Asn Asp Ile
      145             150             155             160

Glu Ser Lys Ser Leu Val Leu Lys Gly Cys Ser Asn Val Ser Asn Ala
      165             170             175

Thr Cys Gln Phe Leu Ser Gly Glu Asn Lys Thr Leu Gly Gly Val Ile
      180             185             190

Phe Arg Lys Phe Glu Cys Ala Asn Val Asn Ser Leu Thr Pro Thr Ser
      195             200             205

Ala Pro Thr Thr Ser His Asn Val Gly Ser Lys Ala Ser Leu Tyr Leu
      210             215             220

Leu Ala Leu Ala Ser Leu Leu Leu Arg Gly Leu Leu Pro
      225             230             235

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&lt;210&gt; 155

&lt;211&gt; 314

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (49)

&lt;223&gt; Xaa equals any one of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (167)

&lt;223&gt; Xaa equals any one of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (314)

&lt;223&gt; Xaa equals stop translation

&lt;400&gt; 155

Met	Asn	Gln	Leu	Ser	Phe	Leu	Leu	Phe	Leu	Ile	Ala	Thr	Thr	Arg	Gly
1				5					10					15	

Trp	Ser	Thr	Asp	Glu	Ala	Asn	Thr	Tyr	Phe	Lys	Glu	Trp	Thr	Cys	Ser
			20					25					30		

Ser	Ser	Pro	Ser	Leu	Pro	Arg	Ser	Cys	Lys	Glu	Ile	Lys	Asp	Glu	Cys
		35					40					45			

Xaa	Ser	Ala	Phe	Asp	Gly	Leu	Tyr	Phe	Leu	Arg	Thr	Glu	Asn	Gly	Val
50						55					60				

Ile	Tyr	Gln	Thr	Phe	Cys	Asp	Met	Thr	Ser	Gly	Gly	Gly	Gly	Trp	Thr
65					70					75					80

Leu	Val	Ala	Ser	Val	His	Glu	Asn	Asp	Met	Arg	Gly	Lys	Cys	Thr	Val
				85					90					95	

Gly	Asp	Arg	Trp	Ser	Ser	Gln	Gln	Gly	Ser	Lys	Ala	Asp	Tyr	Pro	Glu
			100					105					110		

Gly	Asp	Gly	Asn	Trp	Ala	Asn	Tyr	Asn	Thr	Phe	Gly	Ser	Ala	Glu	Ala
		115					120					125			

Ala	Thr	Ser	Asp	Asp	Tyr	Lys	Asn	Pro	Gly	Tyr	Tyr	Asp	Ile	Gln	Ala
		130				135					140				

Lys	Asp	Leu	Gly	Ile	Trp	His	Val	Pro	Asn	Lys	Ser	Pro	Met	Gln	His
145					150					155					160

Trp	Arg	Asn	Ser	Ser	Leu	Xaa	Arg	Tyr	Arg	Thr	Asp	Thr	Gly	Phe	Leu
				165					170					175	

Gln	Thr	Leu	Gly	His	Asn	Leu	Phe	Gly	Ile	Tyr	Gln	Lys	Tyr	Pro	Val
		180						185					190		

Lys	Tyr	Gly	Glu	Gly	Lys	Cys	Trp	Thr	Asp	Asn	Gly	Pro	Val	Ile	Pro
		195					200					205			

Val	Val	Tyr	Asp	Phe	Gly	Asp	Ala	Gln	Lys	Thr	Ala	Ser	Tyr	Tyr	Ser
	210					215					220				

Pro	Tyr	Gly	Gln	Arg	Glu	Phe	Thr	Ala	Gly	Phe	Val	Gln	Phe	Arg	Val
225					230					235					240

Phe	Asn	Asn	Glu	Arg	Ala	Ala	Asn	Ala	Leu	Cys	Ala	Gly	Met	Arg	Val
			245						250					255	

Thr	Gly	Cys	Asn	Thr	Glu	His	His	Cys	Ile	Gly	Gly	Gly	Gly	Tyr	Phe
			260					265						270	

Pro	Glu	Ala	Ser	Pro	Gln	Gln	Cys	Gly	Asp	Phe	Ser	Gly	Phe	Asp	Trp
		275					280					285			

Ser Gly Tyr Gly Thr His Val Gly Tyr Ser Ser Ser Arg Glu Ile Thr  
 290 295 300

Glu Ala Ala Val Leu Leu Phe Tyr Arg Xaa  
 305 310

<210> 156

<211> 99

<212> PRT

<213> Homo sapiens

<220>

<221> misc feature

<222> (17)

<223> Xaa equals any one of the naturally occurring L-amino acids

<220>

<221> misc feature

<222> (24)

<223> Xaa equals any one of the naturally occurring L-amino acids

<220>

<221> misc feature

<222> (99)

<223> Xaa equals stop translation

<400> 156

Met Leu Ala Phe Pro Val Leu Leu Glu Val Ser Trp Ser Val Leu Phe  
 1 5 10 15

Xaa Phe Ser Phe Phe Ser Pro Xaa Pro Ser Ala Pro Gln Pro Pro Thr  
 20 25 30

Pro Ser Arg Ser Val Leu His Ala Arg Cys Ser Asn Val Arg Ser Glu  
 35 40 45

Met Ala Gly Thr Arg Glu Lys Leu Leu Val Ser Phe Val Ser Gly Ser  
 50 55 60

Gly Met Ala Leu Ser Ser Leu Ala Ser Leu Phe Val Leu Phe Glu Leu  
 65 70 75 80

Cys Arg Ser Leu Phe Ser Gln Ala Glu Leu Pro Thr Arg Ser Ile Leu  
 85 90 95

Asp Gln Xaa

<210> 157

<211> 37

<212> PRT

<213> Homo sapiens

<220>

<221> misc feature

<222> (8)

<223> Xaa equals any one of the naturally occurring L-amino acids

<220>  
<221> misc feature  
<222> (19)  
<223> Xaa equals any one of the naturally occurring L-amino acids

<220>  
<221> misc feature  
<222> (28)  
<223> Xaa equals any one of the naturally occurring L-amino acids

<220>  
<221> misc feature  
<222> (37)  
<223> Xaa equals stop translation

<400> 157  
Met Asn Pro Phe Ser Val Phe Xaa Ser Leu Cys Leu Lys Gln Phe Glu  
1 5 10 15  
Asp Val Xaa Leu Phe Leu Gly Leu Met Phe Gly Xaa Ser Leu Asn Gly  
20 25 30  
Gln Glu Gly Thr Xaa  
35

<210> 158  
<211> 23  
<212> PRT  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (23)  
<223> Xaa equals stop translation

<400> 158  
Met Val Ile Phe Ile Ile Leu Leu Thr Cys Phe Gly Phe Ser Asn Gly  
1 5 10 15  
Ser Phe Ser Phe Ser Leu Xaa  
20

<210> 159  
<211> 96  
<212> PRT  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (30)  
<223> Xaa equals any one of the naturally occurring L-amino acids  
  
<220>  
<221> misc feature  
<222> (35)  
<223> Xaa equals any one of the naturally occurring L-amino acids



<220>  
 <221> misc feature  
 <222> (64)  
 <223> Xaa equals any one of the naturally occurring L-amino acids

<220>  
 <221> misc feature  
 <222> (83)  
 <223> Xaa equals any one of the naturally occurring L-amino acids

<400> 159  
 Met Cys Phe Ile Leu Val Val Cys Phe Ala Ser Leu Ile Thr Glu Cys  
           1                  5                  10                  15  
 Pro Cys His Cys Lys Cys Cys Arg Asp Val Gly Arg Gly Xaa Thr Val  
                   20                  25                  30  
 Leu Tyr Xaa Cys Ser Met Val Gln Asn Lys Leu Leu Thr Gln Val Ser  
           35                  40                  45  
 Leu Val Arg Asn Leu Trp Ala Met Glu Val Arg His Pro Ser Cys Xaa  
           50                  55                  60  
 Ser Ile Gly Lys Lys Cys Phe Gln Ile Leu Trp Lys Gly Gly His Gly  
           65                  70                  75                  80  
 Ala Gly Xaa Trp Arg Val Ala Phe Glu Gln Ser Asp Pro Ile Ser Val  
           85                  90                  95

<210> 160  
 <211> 66  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (66)  
 <223> Xaa equals stop translation

<400> 160  
 Met Val Glu Asn Trp Val Leu Glu Glu Ser Pro Gly Arg Leu Leu Ala  
           1                  5                  10                  15  
 Leu Phe Val Val Arg Arg Ala Leu Ala Gln Gly Gln Arg Glu Glu Lys  
           20                  25                  30  
 Gly Gln Pro Ala Ala Val Glu Ser Ala Gly Trp Leu Pro Thr Arg Phe  
           35                  40                  45  
 Leu Ser Ser Gln Asp Ser Leu Pro Leu Ser Ser Arg Ile Ser Asn Gly  
           50                  55                  60  
 Leu Xaa  
           65

<210> 161  
 <211> 222  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (86)  
 <223> Xaa equals any one of the naturally occurring L-amino acids

<400> 161  
 Met His Phe Gln Arg Gln Lys Leu Met Ala Val Thr Glu Tyr Ile Pro  
           1                  5                  10                  15  
 Pro Lys Pro Ala Ile His Pro Ser Cys Leu Pro Ser Pro Pro Ser Pro  
                   20                  25                  30  
 Pro Gln Glu Glu Ile Gly Leu Ile Arg Leu Leu Arg Arg Glu Ile Ala  
           35                  40                  45  
 Ala Val Phe Gln Asp Asn Arg Met Ile Ala Val Cys Gln Asn Val Ala  
           50                  55                  60  
 Leu Ser Ala Glu Asp Lys Leu Leu Met Arg His Gln Leu Arg Lys His  
           65                  70                  75                  80  
 Lys Ile Leu Met Lys Xaa Phe Pro Asn Gln Val Leu Lys Pro Phe Leu  
                   85                  90                  95  
 Glu Asp Ser Lys Tyr Gln Asn Leu Leu Pro Leu Phe Val Gly His Asn  
           100                  105                  110  
 Met Leu Leu Val Ser Glu Glu Pro Lys Val Lys Glu Met Val Arg Ile  
           115                  120                  125  
 Leu Arg Thr Val Pro Phe Leu Pro Leu Leu Gly Gly Cys Ile Asp Asp  
           130                  135                  140  
 Thr Ile Leu Ser Arg Gln Gly Phe Ile Asn Tyr Ser Lys Leu Pro Ser  
           145                  150                  155                  160  
 Leu Pro Leu Val Gln Gly Glu Leu Val Gly Gly Leu Thr Cys Leu Thr  
           165                  170                  175  
 Ala Gln Thr His Ser Leu Leu Gln His Gln Pro Leu Gln Leu Thr Thr  
           180                  185                  190  
 Leu Leu Asp Gln Tyr Ile Arg Glu Gln Arg Glu Lys Asp Ser Val Met  
           195                  200                  205  
 Ser Ala Asn Gly Lys Pro Asp Pro Asp Thr Val Pro Asp Ser  
           210                  215                  220

<210> 162  
 <211> 91  
 <212> PRT  
 <213> Homo sapiens

<220>

<221> misc feature  
 <222> (53)  
 <223> Xaa equals any one of the naturally occurring L-amino acids

<400> 162

Met Val Val Asp Gln Lys Glu Asp Leu Ile Thr Gly Leu Gly Ile Lys  
 1 5 10 15

Met Val Arg Lys Trp Leu Gln Gly Ser Gln Ala Trp Pro Leu Glu Arg  
 20 25 30

Glu Glu Arg Glu Gly Leu Gly Ser Leu Cys Thr Cys Cys Pro Trp Gly  
 35 40 45

Leu Val Arg Phe Xaa Glu Ser Leu Thr His Phe Thr Gly Glu Ala Ile  
 50 55 60

Glu Pro Leu Arg Ala Glu Val Thr Asp Pro Lys His Pro Cys Ser Cys  
 65 70 75 80

Val Ala Glu Pro Glu Val Lys Ser Arg Ser Leu  
 85 90

<210> 163  
 <211> 74  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (51)  
 <223> Xaa equals any one of the naturally occurring L-amino acids

<400> 163

Met Glu Asn Asp Trp Gly Phe Gln Thr Thr Phe Phe Ser Leu Gly Leu  
 1 5 10 15

Tyr Leu Phe Thr Ile Trp Trp Ser Thr Val Gly Leu Pro Trp Thr Ser  
 20 25 30

Ser Thr Gln Arg Glu Leu Asp Met Lys Leu Glu Ala Ala Ala Leu Glu  
 35 40 45

Gly Lys Xaa Gly Ser Leu Gly Gln Pro Arg Pro Trp Gln Glu Glu Ser  
 50 55 60

Leu Pro Leu Gly Val Leu Asp Gly His Val  
 65 70

<210> 164  
 <211> 78  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (69)  
 <223> Xaa equals any one of the naturally occurring L-amino acids

<220>  
<221> misc feature  
<222> (78)  
<223> Xaa equals stop translation  
  
<400> 164  
Met Thr Gly Gln Ile Pro Arg Leu Ser Lys Val Asn Leu Phe Thr Leu  
1 5 10 15  
Leu Ser Leu Trp Met Glu Leu Phe Pro Ala Glu Ala Gln Arg Gln Lys  
20 25 30  
Ser Gln Lys Asn Glu Glu Gly Lys His Gly Pro Leu Gly Asp Asn Glu  
35 40 45  
Glu Arg Thr Arg Val Ser Thr Asp Lys Arg Gln Asp Tyr Trp Glu Gln  
50 55 60  
Leu Arg Cys Leu Xaa Glu Arg Phe Thr Ile Thr Ala Gly Xaa  
65 70 75

<210> 165  
<211> 38  
<212> PRT  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (38)  
<223> Xaa equals stop translation

<400> 165  
Met Ala Phe Leu Leu Thr Leu Val Pro Leu Leu Pro Ser Arg Cys Leu  
1 5 10 15  
Gly Leu Glu Glu Met Ala Val Pro Asn Ser Thr Cys Ile Ser Pro Phe  
20 25 30  
Ser Cys Cys Tyr Gly Xaa  
35

<210> 166  
<211> 45  
<212> PRT  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (45)  
<223> Xaa equals stop translation

<400> 166  
Met Phe His Val Phe Val Leu Leu Leu Thr Phe Ile Ala Leu Ser Pro  
1 5 10 15  
Ser Gly Ile Arg Leu Leu Phe Gly Phe Ile Gln Lys Gly Leu Asn Leu  
20 25 30

Asn Ser Phe Met Phe Arg Leu Glu Leu Leu His Phe Xaa  
35 40 45

<210> 167

<211> 39

<212> PRT

<213> Homo sapiens

<220>

<221> misc feature

<222> (39)

<223> Xaa equals stop translation

<400> 167

Met Thr Ser Leu Pro Ile Leu Ala Phe Gly Ala Val Tyr Trp Pro Asp  
1 5 10 15

Leu Ala Ser His Ser Phe Ser Pro Ser Arg Ser Leu Ala Gln Thr Pro  
20 25 30

His Met Ser Val Ser Gly Xaa  
35

<210> 168

<211> 174

<212> PRT

<213> Homo sapiens

<220>

<221> misc feature

<222> (83)

<223> Xaa equals any one of the naturally occurring L-amino acids

<220>

<221> misc feature

<222> (110)

<223> Xaa equals any one of the naturally occurring L-amino acids

<220>

<221> misc feature

<222> (115)

<223> Xaa equals any one of the naturally occurring L-amino acids

<220>

<221> misc feature

<222> (118)

<223> Xaa equals any one of the naturally occurring L-amino acids

<220>

<221> misc feature

<222> (168)

<223> Xaa equals any one of the naturally occurring L-amino acids

<220>

<221> misc feature

<222> (174)

<223> Xaa equals stop translation

&lt;400&gt; 168

Met Gln Leu Ile Pro Leu Glu Gln Leu Cys Met Leu Leu Leu Met Ser  
 1 5 10 15

Asp Asn Val Asp Arg Cys Phe Glu Thr Cys Pro Pro Arg Thr Phe Leu  
 20 25 30

Pro Ala Leu Cys Lys Ile Phe Leu Asp Glu Ser Ala Pro Asp Asn Val  
 35 40 45

Leu Glu Val Thr Ala Arg Ala Ile Thr Tyr Tyr Leu Asp Val Ser Ala  
 50 55 60

Glu Cys Thr Arg Arg Ile Val Gly Val Asp Gly Ala Ile Lys Ala Leu  
 65 70 75 80

Cys Asn Xaa Leu Val Val Val Glu Leu Asn Asn Arg Thr Ser Arg Asp  
 85 90 95

Leu Ala Glu Gln Cys Val Lys Val Leu Glu Leu Ile Cys Xaa Pro Glu  
 100 105 110

Ser Gly Xaa Val Phe Xaa Ala Gly Gly Leu Asn Arg Val Ala Tyr Leu  
 115 120 125

Pro Ser Val Asn Ser Gly His Leu Val His Lys Asp Thr Leu His Ser  
 130 135 140

Ala Met Ala Val Val Ser Arg Leu Cys Gly Lys Met Glu Pro Gln Asp  
 145 150 155 160

Ser Ser Leu Glu Ile Cys Val Xaa Ser Leu Ser Ser Leu Xaa  
 165 170

&lt;210&gt; 169

&lt;211&gt; 55

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (55)

&lt;223&gt; Xaa equals stop translation

&lt;400&gt; 169

Met Phe Glu Asp Thr Leu Arg Thr Leu Tyr Ile Leu Leu Phe Tyr Leu  
 1 5 10 15

Arg Tyr Ile Cys Leu Leu Ser Pro His Ile Ala Leu Met Thr Leu Ile  
 20 25 30

Leu Ile Asp Gly Phe Leu Gln Cys Tyr Tyr Cys Ala Leu His Val Pro  
 35 40 45

Cys Ile Ile Ala Phe Leu Xaa  
 50 55

<210> 170  
 <211> 344  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (126)  
 <223> Xaa equals any one of the naturally occurring L-amino acids

<220>  
 <221> misc feature  
 <222> (128)  
 <223> Xaa equals any one of the naturally occurring L-amino acids

<400> 170  
 Met Glu Lys Ile Gly Ser Ser Leu Pro Gln Asp Asp Ala Pro Lys  
   1                  5                  10                  15  
 Lys Gln Ala Leu Tyr Leu Met Phe Asp Thr Ser Gln Glu Ser Pro Val  
           20                  25                  30  
 Lys Ser Ser Pro Val Arg Met Ser Glu Ser Pro Thr Pro Cys Ser Gly  
       35                  40                  45  
 Ser Ser Phe Glu Glu Thr Glu Ala Leu Val Asn Thr Ala Ala Lys Asn  
   50                  55                  60  
 Gln His Pro Val Pro Arg Gly Leu Ala Pro Asn Gln Glu Ser His Leu  
  65                  70                  75                  80  
 Gln Val Pro Glu Lys Ser Ser Gln Lys Glu Leu Glu Ala Met Gly Leu  
           85                  90                  95  
 Gly Thr Pro Ser Glu Ala Ile Glu Ile Arg Glu Ala Ala His Pro Thr  
      100                  105                  110  
 Asp Val Ser Ile Ser Lys Thr Ala Leu Tyr Ser Arg Ile Xaa Thr Xaa  
  115                  120                  125  
 Glu Val Glu Lys Pro Ala Gly Leu Leu Phe Gln Gln Pro Asp Leu Asp  
  130                  135                  140  
 Ser Ala Leu Gln Ile Ala Arg Ala Glu Ile Ile Thr Lys Glu Arg Glu  
 145                  150                  155                  160  
 Val Ser Glu Trp Lys Asp Lys Tyr Glu Glu Ser Arg Arg Glu Val Met  
      165                  170                  175  
 Glu Met Arg Lys Ile Val Ala Glu Tyr Glu Lys Thr Ile Ala Gln Met  
      180                  185                  190  
 Ile Glu Asp Glu Gln Arg Glu Lys Ser Val Ser His Gln Thr Val Gln  
  195                  200                  205  
 Gln Leu Val Leu Glu Lys Glu Gln Ala Leu Ala Asp Leu Asn Ser Val  
  210                  215                  220  
 Glu Lys Ser Leu Ala Asp Leu Phe Arg Arg Tyr Glu Lys Met Lys Glu  
 225                  230                  235                  240

Val Leu Glu Gly Phe Arg Lys Asn Glu Glu Val Leu Lys Arg Cys Ala  
 245 250 255

Gln Glu Tyr Leu Ser Arg Val Lys Lys Glu Glu Gln Arg Tyr Gln Ala  
 260 265 270

Leu Lys Val His Ala Glu Glu Lys Leu Asp Arg Ala Asn Ala Glu Ile  
 275 280 285

Ala Gln Val Arg Gly Lys Ala Gln Gln Glu Gln Ala Ala His Gln Ala  
 290 295 300

Ser Leu Arg Lys Glu Gln Leu Arg Val Asp Ala Leu Glu Arg Thr Leu  
 305 310 315 320

Glu Gln Lys Asn Lys Glu Ile Glu Glu Leu Thr Lys Ile Cys Asp Glu  
 325 330 335

Leu Ile Ala Lys Met Gly Lys Ser  
 340

&lt;210&gt; 171

&lt;211&gt; 90

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (90)

&lt;223&gt; Xaa equals stop translation

&lt;400&gt; 171

Met Tyr His Tyr Ala Trp Leu Ile Phe Val Phe Leu Val Glu Met Gly  
 1 5 10 15

Phe Cys His Val Gly Gln Ala Gly Leu Lys Leu Leu Thr Ser Ser Asp  
 20 25 30

Pro Pro Ala Ser Ala Ser Gln Ser Ala Gly Ile Thr Gly Val Ser His  
 35 40 45

His Ala Trp Gly Lys Arg Tyr Phe Gln Asn Ile Val Asn Asn Phe Ser  
 50 55 60

Pro Lys Pro Arg Gln Gly Leu Ile Leu Leu Pro Arg Leu Glu Trp Gln  
 65 70 75 80

Gly His His Arg Ser Ser Leu Gln Pro Xaa  
 85 90

&lt;210&gt; 172

&lt;211&gt; 104

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 172

Met Leu Cys Pro Asn His Gly Leu Phe Pro Asp Pro Gly Phe Gln Cys



1                    5                    10                    15  
 Pro Pro Leu Phe Gln Glu Val Gln Arg Asp Ala Pro His Arg Lys Gly  
                   20                    25                    30  
 Ser Ala Thr Val Leu Pro Arg Cys Pro Pro Trp Val Pro Ser Leu Lys  
                   35                    40                    45  
 His Arg Thr Ser His Thr Ser Ser Pro Ala Val Pro Leu Ile Leu Val  
                   50                    55                    60  
 Pro Arg Leu Pro Ser Leu Gln Leu His Ser Phe Ile Gln His Ser Leu  
                   65                    70                    75                    80  
 Gly Asp Phe Tyr Ile Asp Thr Pro Arg Thr Glu Ala Trp Gly Lys Asp  
                   85                    90                    95  
 Asp Gln Glu His Val Pro Ser Arg  
                   100

&lt;210&gt; 173

&lt;211&gt; 42

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (42)

&lt;223&gt; Xaa equals stop translation

&lt;400&gt; 173

Met Ser Val Leu Phe Val Ala Val Ser Leu Leu Ser Ser Ile Val Pro  
 1                    5                    10                    15  
 Asp Ile Gln Tyr Arg Leu Lys Thr Tyr Leu His Ile Asp Leu Trp Lys  
                   20                    25                    30  
 Thr Asp Thr Gln Val Leu Lys Asn Lys Xaa  
                   35                    40

&lt;210&gt; 174

&lt;211&gt; 47

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (47)

&lt;223&gt; Xaa equals stop translation

&lt;400&gt; 174

Met Met Leu Gly Leu Phe Ser Pro Leu Cys Leu Val Thr Gly Ile Ala  
 1                    5                    10                    15  
 Glu Gly Arg Ala Glu Asp Ala Ser Leu His Asp Ile Cys Thr Thr Gln  
                   20                    25                    30  
 His Thr Leu Thr Phe Thr Pro Ser Tyr Pro Val Gly Gly Ser Xaa

35 40 45

<210> 175  
<211> 73  
<212> PRT  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (44)  
<223> Xaa equals any one of the naturally occurring L-amino acids

<220>  
<221> misc feature  
<222> (69)  
<223> Xaa equals any one of the naturally occurring L-amino acids

<400> 175  
Met Ser Phe Ser Leu Ala His Val Lys Thr Gly Gln Gly Pro Arg Leu  
1 5 10 15

Thr Glu Ala Leu Gln Tyr Ile Ala Ser Lys Ile Ala Val Gly Val Thr  
20 25 30

Ser Ser Gln Lys Ser Gly Glu Glu Arg Ala Met Xaa Thr Gln Glu Leu  
35 40 45

Leu Met Asp Gln Ala Trp Asp Ser Val Cys His Phe His Gln His Pro  
50 55 60

Thr His Gln Asn Xaa Val Thr Gly Pro  
65 70

<210> 176  
<211> 29  
<212> PRT  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (29)  
<223> Xaa equals stop translation

<400> 176  
Met Leu Ser Leu Asp Phe Pro Leu Ile Leu Leu Gly Leu Asn Leu His  
1 5 10 15

Ile Ala Leu Leu Ser Leu Leu Val Pro Arg Leu Ser Xaa  
20 25

<210> 177  
<211> 67  
<212> PRT  
<213> Homo sapiens

<400> 177  
Met Ile Phe Arg Asn Gly Val Arg Leu Val Phe Val Phe Val Leu Phe

1                    5                    10                    15  
 Tyr Thr Ser Thr Gln Ser Leu Phe Asn Ser Leu Gln Thr Ala Glu Tyr  
                   20                    25                    30  
 Val Leu Phe Cys Gln Gln Arg Leu Ser Leu Tyr Glu Pro Ser His Val  
                   35                    40                    45  
 Leu Cys Leu Cys Met Ser Pro His Arg Lys His Thr Arg Glu Ser Asp  
                   50                    55                    60  
 Thr Ser Gly  
                   65

<210> 178  
 <211> 24  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (24)  
 <223> Xaa equals stop translation

<400> 178  
 Met Asn Phe Leu Leu Leu Ile Phe Pro Tyr Phe Ser Ser Leu Leu Gly  
                   1                    5                    10                    15  
 Glu Val Glu Val Val Lys Cys Xaa  
                   20

<210> 179  
 <211> 31  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (31)  
 <223> Xaa equals stop translation

<400> 179  
 Met Ser Pro Gly Arg Val Ser Val Val Ser Leu Gln Gly Ser Gln Leu  
                   1                    5                    10                    15  
 Cys Leu Leu Val Ser Ile Ala Ile Met Gly Leu Leu Leu Phe Xaa  
                   20                    25                    30

<210> 180  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (11)  
 <223> Xaa equals stop translation

100

&lt;400&gt; 180

Met Ala Tyr Ala Phe His Arg Thr Ser Thr Xaa

1 5 10

&lt;210&gt; 181

&lt;211&gt; 32

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (32)

&lt;223&gt; Xaa equals stop translation

&lt;400&gt; 181

Met Ser Val Lys Val Gly Ser Leu Leu Val Leu Val Tyr Phe Thr Leu

1 5 10 15

Gly Pro Val Val Ala Glu Leu Glu Val Thr Leu Pro Ser His Ser Xaa

20 25 30

&lt;210&gt; 182

&lt;211&gt; 36

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (36)

&lt;223&gt; Xaa equals stop translation

&lt;400&gt; 182

Met Ile Val Ile Thr Ser Ile Leu Ser Ser Leu Ala Ser Leu Leu Leu

1 5 10 15

Leu Ala Phe Leu Ala Ala Ser Thr Ala Arg Leu Ser Pro Gln Ser Leu

20 25 30

Pro Glu Thr Xaa

35

&lt;210&gt; 183

&lt;211&gt; 35

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (35)

&lt;223&gt; Xaa equals stop translation

&lt;400&gt; 183

Met Ser Gly Leu Glu Ser Ala Arg Val Leu Leu Cys Ala Leu Gly Ser

1                    5                    10                    15  
Phe Leu Leu Asn Ser Leu Leu Ser Thr Phe Arg Leu Asn Ser Ser Ala  
                    20                    25                    30

Pro Ser Xaa  
                    35

<210> 184  
<211> 29  
<212> PRT  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (29)  
<223> Xaa equals stop translation

<400> 184  
Met His Ser Ile Ile Val Lys Glu Leu Ile Val Thr Phe Phe Leu Gly  
                    1                    5                    10                    15

Ile Thr Val Leu Leu Leu Met Gln Arg Ser Leu Xaa  
                    20                    25

<210> 185  
<211> 6  
<212> PRT  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (6)  
<223> Xaa equals stop translation

<400> 185  
Met Gly Tyr Leu Asn Xaa  
                    1                    5

<210> 186  
<211> 53  
<212> PRT  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (53)  
<223> Xaa equals stop translation

<400> 186  
Asp Leu Thr Ser Leu Leu Phe Tyr Leu Ala Gly Cys Phe Ser Ser Cys  
                    1                    5                    10                    15

Arg Leu Gly Gln Gly Thr Pro Gly Ser Leu Pro Trp Thr Ser Asn Glu  
                    20                    25                    30

Glu Gly Ile Ile Gln Gly Pro Thr Pro Met Phe Trp Asn Leu Thr Pro

35                      40                      45  
 Phe Ser Gly Thr Xaa  
 50  
  
 <210> 187  
 <211> 406  
 <212> PRT  
 <213> Homo sapiens  
  
 <220>  
 <221> misc feature  
 <222> (273)  
 <223> Xaa equals any one of the naturally occurring L-amino acids  
  
 <220>  
 <221> misc feature  
 <222> (406)  
 <223> Xaa equals stop translation  
  
 <400> 187  
 Met Leu Leu Leu Trp Val Ser Val Val Ala Ala Leu Ala Leu Ala Val  
   1                      5                      10                      15  
  
 Leu Ala Pro Gly Ala Gly Glu Gln Arg Arg Arg Ala Ala Lys Ala Pro  
                     20                      25                      30  
  
 Asn Val Val Leu Val Val Ser Asp Ser Tyr Asp Gly Arg Leu Thr Phe  
                     35                      40                      45  
  
 His Pro Gly Ser Gln Val Val Lys Leu Pro Phe Ile Asn Phe Met Lys  
   50                      55                      60  
  
 Thr Arg Gly Thr Ser Phe Leu Asn Ala Tyr Thr Asn Ser Pro Ile Cys  
   65                      70                      75                      80  
  
 Cys Pro Ser Arg Ala Ala Met Trp Ser Gly Leu Phe Thr His Leu Thr  
                     85                      90                      95  
  
 Glu Ser Trp Asn Asn Phe Lys Gly Leu Asp Pro Asn Tyr Thr Thr Trp  
                     100                      105                      110  
  
 Met Asp Val Met Glu Arg His Gly Tyr Arg Thr Gln Lys Phe Gly Lys  
   115                      120                      125  
  
 Leu Asp Tyr Thr Ser Gly His His Ser Ile Ser Asn Arg Val Glu Ala  
   130                      135                      140  
  
 Trp Thr Arg Asp Val Ala Phe Leu Leu Arg Gln Glu Gly Arg Pro Met  
   145                      150                      155                      160  
  
 Val Asn Leu Ile Arg Asn Arg Thr Lys Val Arg Val Met Glu Arg Asp  
                     165                      170                      175  
  
 Trp Gln Asn Thr Asp Lys Ala Val Asn Trp Leu Arg Lys Glu Ala Ile  
                     180                      185                      190  
  
 Asn Tyr Thr Glu Pro Phe Val Ile Tyr Leu Gly Leu Asn Leu Pro His  
   195                      200                      205

Pro Tyr Pro Ser Pro Ser Ser Gly Glu Asn Phe Gly Ser Ser Thr Phe  
 210 215 220  
 His Thr Ser Leu Tyr Trp Leu Glu Lys Val Ser His Asp Ala Ile Lys  
 225 230 235 240  
 Ile Pro Lys Trp Ser Pro Leu Ser Glu Met His Pro Val Asp Tyr Tyr  
 245 250 255  
 Ser Ser Tyr Thr Lys Asn Cys Thr Gly Arg Phe Thr Lys Lys Glu Ile  
 260 265 270  
 Xaa Asn Ile Arg Ala Phe Tyr Tyr Ala Met Cys Ala Glu Thr Asp Ala  
 275 280 285  
 Met Leu Gly Glu Ile Ile Leu Ala Leu His Gln Leu Asp Leu Leu Gln  
 290 295 300  
 Lys Thr Ile Val Ile Tyr Ser Ser Asp His Gly Glu Leu Ala Met Glu  
 305 310 315 320  
 His Arg Gln Phe Tyr Lys Met Ser Met Tyr Glu Ala Ser Ala His Val  
 325 330 335  
 Pro Leu Leu Met Met Gly Pro Gly Ile Lys Ala Gly Leu Gln Val Ser  
 340 345 350  
 Asn Val Val Ser Leu Val Asp Ile Tyr Pro Thr Met Leu Asp Ile Ala  
 355 360 365  
 Gly Ile Pro Leu Pro Gln Asn Leu Ser Gly Tyr Ser Ser Leu Pro Leu  
 370 375 380  
 Ser Ser Glu Thr Phe Lys Asn Glu His Lys Val Lys Asn Leu His Pro  
 385 390 395 400  
 Pro Trp Ile Thr Glu Xaa  
 405

&lt;210&gt; 188

&lt;211&gt; 37

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (37)

&lt;223&gt; Xaa equals stop translation

&lt;400&gt; 188

Met Asn Gly Leu Val Arg Pro Val Glu Leu Asn Ser Leu Leu Leu Pro  
 1 5 10 15

Val Val Arg Tyr Gln Val Ala Gln Pro Gln Lys Leu Leu Asn Val Phe  
 20 25 30

Val Gly Gly Leu Xaa  
 35

104

<210> 189  
 <211> 57  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (51)  
 <223> Xaa equals any one of the naturally occurring L-amino acids

<400> 189  
 Met Lys Ala Leu Val Gly Asn Ser Pro Pro Val Gly Asp Ser Gly Thr  
 1 5 10 15  
 Gln Pro Pro Ser Ala Leu Arg Leu Cys Leu Leu Lys Val Leu Arg Val  
 20 25 30  
 Leu Ser Met Tyr Leu Ala Asn Gly Glu Arg Val Trp Arg Thr His Lys  
 35 40 45  
 Arg Val Xaa His His Val Leu Arg Gly  
 50 55

<210> 190  
 <211> 128  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (127)  
 <223> Xaa equals any one of the naturally occurring L-amino acids

<220>  
 <221> misc feature  
 <222> (128)  
 <223> Xaa equals stop translation

<400> 190  
 Met Phe Val Leu Leu Tyr Val Thr Ser Phe Ala Ile Cys Ala Ser Gly  
 1 5 10 15  
 Gln Pro Arg Gly Asn Gln Leu Lys Gly Glu Asn Tyr Ser Pro Arg Tyr  
 20 25 30  
 Ile Cys Ser Ile Pro Gly Leu Pro Gly Pro Pro Gly Pro Pro Gly Ala  
 35 40 45  
 Asn Gly Ser Pro Gly Pro His Gly Arg Ile Gly Leu Pro Gly Arg Asp  
 50 55 60  
 Gly Arg Asp Gly Arg Lys Gly Glu Lys Gly Glu Lys Gly Thr Ala Gly  
 65 70 75 80  
 Leu Arg Gly Lys Thr Gly Pro Leu Gly Leu Ala Gly Glu Lys Gly Asp  
 85 90 95



105

Gln Gly Glu Thr Gly Lys Lys Gly Pro Ile Gly Pro Glu Gly Glu Lys  
                   100                  105                  110

Gly Glu Val Gly Pro Ile Gly Pro Pro Gly Pro Lys Gly Asp Xaa Xaa  
           115                  120                  125

&lt;210&gt; 191

&lt;211&gt; 21

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (21)

&lt;223&gt; Xaa equals stop translation

&lt;400&gt; 191

Met Lys Phe Ile Met Leu Leu Leu Leu Pro Ser Ile Phe Pro Thr Thr  
   1                  5                  10                  15

Val Glu Met Ile Xaa  
                   20

&lt;210&gt; 192

&lt;211&gt; 143

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (92)

&lt;223&gt; Xaa equals any one of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (136)

&lt;223&gt; Xaa equals any one of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (138)

&lt;223&gt; Xaa equals any one of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (143)

&lt;223&gt; Xaa equals stop translation

&lt;400&gt; 192

Met Cys Ala Phe Pro Trp Leu Leu Leu Leu Leu Leu Gln Glu Gly  
   1                  5                  10                  15

Ser Gln Arg Arg Leu Trp Arg Trp Cys Gly Ser Glu Glu Val Val Ala  
           20                  25                  30

106

Val Leu Gln Glu Ser Ile Ser Leu Pro Leu Glu Ile Pro Pro Asp Glu  
35 40 45

Glu Val Glu Asn Ile Ile Trp Ser Ser His Lys Ser Leu Ala Thr Val  
50 55 60

Val Pro Gly Lys Glu Gly His Pro Ala Thr Ile Met Val Thr Asn Pro  
65 70 75 80

His Tyr Gln Gly Gln Val Ser Phe Leu Asp Pro Xaa Tyr Ser Leu His  
85 90 95

Ile Ser Asn Leu Ser Trp Glu Asp Ser Gly Leu Tyr Gln Ala Gln Val  
100 105 110

Asn Leu Arg Thr Ser Gln Ile Ser Thr Met Gln Gln Tyr Asn Leu Cys  
115 120 125

Val Tyr Arg Trp Leu Ser Glu Xaa Pro Xaa His Cys Glu Leu Xaa  
130 135 140

&lt;210&gt; 193

&lt;211&gt; 110

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (110)

&lt;223&gt; Xaa equals stop translation

&lt;400&gt; 193

Met Ile Lys Lys Asp Lys Tyr His Lys Lys Val Phe Leu Phe Gly Trp  
1 5 10 15

Phe Phe Cys Leu Phe Val Phe Phe Leu Arg Leu Ser Leu Ser Leu Leu  
20 25 30

Pro Lys Leu Glu Cys Asn Leu Gly Ser Leu Gln Pro Pro Pro Pro Arg  
35 40 45

Phe Gln Arg Phe Ser Cys Leu Ser Leu Leu Asn Ser Trp Asp Tyr Arg  
50 55 60

Arg Pro Pro Pro His Leu Ala Asn Phe Cys Val Val Ser Arg Gly Gly  
65 70 75 80

Val Ser Ser Cys Trp Pro Gly Trp Ser Arg Thr Pro Asp Leu Met Ile  
85 90 95

Arg Leu Pro Arg Pro Pro Arg Val Leu Gly Leu Gln Ala Xaa  
100 105 110

&lt;210&gt; 194

&lt;211&gt; 80

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

<220>  
 <221> misc feature  
 <222> (73)  
 <223> Xaa equals any one of the naturally occurring L-amino acids

<220>  
 <221> misc feature  
 <222> (78)  
 <223> Xaa equals any one of the naturally occurring L-amino acids

<400> 194  
 Met Phe Leu Thr Ile Ile Val Cys Gly Met Val Ala Ala Leu Ser Ala  
           1                  5                  10                  15  
 Ile Arg Ala Asn Cys His Gln Glu Pro Ser Val Cys Leu Gln Ala Ala  
                   20                  25                  30  
 Cys Pro Glu Ser Trp Ile Gly Phe Gln Arg Lys Cys Phe Tyr Phe Ser  
           35                  40                  45  
 Asp Asp Thr Lys Asn Trp Thr Ser Ser Gln Arg Phe Cys Asp Ser Gln  
           50                  55                  60  
 Asp Ala Asp Leu Ala Gln Val Glu Xaa Phe Gln Glu Leu Xaa Arg Lys  
           65                  70                  75                  80

<210> 195  
 <211> 210  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (210)  
 <223> Xaa equals stop translation

<400> 195  
 Met Cys Pro Leu Trp Arg Leu Leu Ile Phe Leu Gly Leu Leu Ala Leu  
           1                  5                  10                  15  
 Pro Leu Ala Pro His Lys Gln Pro Trp Pro Gly Leu Ala Gln Ala His  
           20                  25                  30  
 Arg Asp Asn Lys Ser Thr Leu Ala Arg Ile Ile Ala Gln Gly Leu Ile  
           35                  40                  45  
 Lys His Asn Ala Glu Ser Arg Ile Gln Asn Ile His Phe Gly Asp Arg  
           50                  55                  60  
 Leu Asn Ala Ser Ala Gln Val Ala Pro Gly Leu Val Gly Trp Leu Ile  
           65                  70                  75                  80  
 Ser Gly Arg Lys His Gln Gln Gln Gln Glu Ser Ser Ile Asn Ile Thr  
                   85                  90                  95  
 Asn Ile Gln Leu Asp Cys Gly Gly Ile Gln Ile Ser Phe His Lys Glu

108

100                      105                      110  
 Trp Phe Ser Ala Asn Ile Ser Leu Glu Phe Asp Leu Glu Leu Arg Pro  
     115                      120                      125  
 Ser Phe Asp Asn Asn Ile Ile Lys Met Cys Ala His Met Ser Ile Val  
     130                      135                      140  
 Val Glu Phe Trp Leu Glu Lys Asp Glu Phe Gly Arg Arg Asp Leu Val  
     145                      150                      155                      160  
 Ile Gly Lys Cys Asp Ala Glu Pro Ser Ser Val His Val Ala Ile Leu  
                     165                      170                      175  
 Thr Glu Ala Ile Pro Pro Lys Met Asn Gln Phe Leu Tyr Asn Leu Lys  
                     180                      185                      190  
 Glu Asn Leu Gln Lys Val Leu Pro His Met Val Glu Ser Gln Pro Leu  
                     195                      200                      205  
 Ala Xaa  
     210

<210> 196  
 <211> 149  
 <212> PRT  
 <213> Homo sapiens  
  
 <220>  
 <221> misc feature  
 <222> (61)  
 <223> Xaa equals any one of the naturally occurring L-amino acids  
  
 <220>  
 <221> misc feature  
 <222> (142)  
 <223> Xaa equals any one of the naturally occurring L-amino acids  
  
 <220>  
 <221> misc feature  
 <222> (149)  
 <223> Xaa equals stop translation

<400> 196  
 Met Arg Lys Ile Ala Gln Cys Ala Pro Gly Val Val Glu Leu Val Leu  
     1                      5                      10                      15  
 Ile Pro Leu Arg Gln Arg Leu Glu Glu Arg Gln Arg Arg Arg Lys Gln  
                     20                      25                      30  
 Gly Ala Gly Ser Leu Gln Glu Leu Ala Pro Gln Asp Gly Ser Gly Tyr  
                     35                      40                      45  
 Met Asp Val Gly Val Ser Gln Lys Ala Arg Gly Glu Xaa Val Pro Asp  
                     50                      55                      60  
 Pro Gln Gly Gly Gly Gln Leu Ser Trp Asp Arg Pro Pro Ala Pro Arg  
     65                      70                      75                      80

109

Pro Pro Ala Tyr Asn Arg Ala Leu Gln Gly Asp Pro Ser Phe Val Leu  
                     85                    90                    95

Gln Ile Ala Glu Lys Glu Gln Glu Leu Leu Ala Ser Gln Glu Thr Val  
                     100                    105                    110

Gln Val Leu Gln Met Lys Val Arg Arg Leu Glu His Leu Leu Gln Leu  
                     115                    120                    125

Lys Asn Val Arg Ile Glu Asn Leu Ser Arg Arg Leu Gln Xaa Ala Glu  
                     130                    135                    140

Arg Lys Gln Arg Xaa  
 145

<210> 197  
 <211> 36  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (36)  
 <223> Xaa equals stop translation

<400> 197  
 Met His Ile Thr Ser Leu Val Gly Ala Gly Thr Leu Met Val Leu Leu  
       1                    5                    10                    15

Leu Leu Ile Leu Leu Glu Cys Phe Phe Val Ala Glu Ala Leu Val  
                     20                    25                    30

Met Arg Ser Xaa  
                     35

<210> 198  
 <211> 258  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (258)  
 <223> Xaa equals stop translation

<400> 198  
 Met Ala Ala Leu Thr Thr Val Val Val Ala Ala Ala Ala Thr Ala Val  
       1                    5                    10                    15

Ala Gly Ala Val Ala Gly Ala Gly Ala Ala Thr Gly Thr Gly Val Gly  
                     20                    25                    30

Ala Thr Pro Ala Pro Gln Gln Ser Asp Gly Cys Phe Ser Thr Ser Gly  
                     35                    40                    45

Gly Ile Arg Pro Phe His Leu Gln Asn Trp Lys Gln Lys Val Asn Gln  
                     50                    55                    60

110

Thr Lys Lys Ala Glu Phe Val Arg Thr Ala Glu Lys Phe Lys Asn Gln  
 65 70 75 80  
 Val Ile Asn Met Glu Lys Asp Lys His Ser His Phe Tyr Asn Gln Lys  
 85 90 95  
 Ser Asp Phe Arg Phe Glu His Ser Met Leu Glu Glu Leu Glu Asn Lys  
 100 105 110  
 Leu Ile His Ser Arg Lys Thr Glu Arg Ala Lys Phe Gln Gln Gln Leu  
 115 120 125  
 Ala Lys Ile His Asn Asn Val Lys Lys Leu Gln His Gln Leu Lys Asp  
 130 135 140  
 Val Lys Pro Thr Pro Asp Phe Val Glu Lys Leu Arg Glu Met Met Glu  
 145 150 155 160  
 Glu Ile Glu Asn Ala Ile Asn Thr Phe Lys Glu Glu Gln Arg Leu Ile  
 165 170 175  
 Tyr Glu Glu Leu Ile Lys Glu Glu Lys Thr Thr Asn Asn Glu Leu Ser  
 180 185 190  
 Ala Ile Ser Arg Lys Ile Asp Thr Trp Ala Leu Gly Asn Ser Glu Thr  
 195 200 205  
 Glu Lys Ala Phe Arg Ala Ile Ser Ser Lys Val Pro Val Asp Lys Val  
 210 215 220  
 Thr Pro Ser Thr Leu Pro Glu Glu Val Leu Asp Phe Glu Lys Phe Leu  
 225 230 235 240  
 Gln Gln Thr Gly Gly Arg Gln Gly Ala Trp Asp Val Ile Thr Arg Thr  
 245 250 255

Leu Xaa

&lt;210&gt; 199

&lt;211&gt; 59

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (11)

&lt;223&gt; Xaa equals any one of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (59)

&lt;223&gt; Xaa equals stop translation

&lt;400&gt; 199

Met Leu Cys Leu Leu Val Leu Thr Gly Leu Xaa Val Leu Ile Val Gly  
 1 5 10 15

Ile His Ile Leu Glu Leu Leu Ile Asp Glu Ala Ala Met Pro Arg Gly

111

20 25 30  
 Met Gln Gly Thr Ser Leu Gly Gln Val Ser Phe Ser Lys Leu Gly Ser  
 35 40 45

Phe Ala Ser Ser Ala Ser Leu Ser Ala Arg Xaa  
 50 55

<210> 200  
 <211> 34  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (34)  
 <223> Xaa equals stop translation

<400> 200  
 Met Phe Phe Val Leu Leu Cys Phe Trp Leu Phe Pro Phe Ser Lys Asn  
 1 5 10 15

Ser Pro Leu Trp Gly Met Leu Arg Ser Ser Phe Phe Ile Ser Ile Asn  
 20 25 30

Leu Xaa

<210> 201  
 <211> 26  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (26)  
 <223> Xaa equals stop translation

<400> 201  
 Met Ser Leu Ile Leu Leu Leu Ser Val Thr Leu Leu His Leu Ser Phe  
 1 5 10 15

Ser Val Gly Phe Phe Leu Phe Arg Leu Xaa  
 20 25

<210> 202  
 <211> 34  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (34)  
 <223> Xaa equals stop translation

<400> 202  
 Met Lys Ser Val Ile Phe Ile Gln Ser Val Ile Leu Phe Phe Leu Pro

112

1 5 10 15  
Met Ser Gly Asp His Gln Gly Ile Ser Gly Leu Asp Glu Leu Pro Gln  
20 25 30

Ala Xaa

<210> 203  
<211> 58  
<212> PRT  
<213> Homo sapiens

<400> 203  
Met Ser Ser Phe Leu Arg Val Ile Phe Ile Pro Asn Ile Lys Val Ile  
1 5 10 15

Phe Leu Pro Pro Gly Thr Thr Ser Leu Ile His Thr Met Asp Gln Gly  
20 25 30

Val Ile Ala Ala Phe Lys Phe Tyr Tyr Leu Arg Arg Glu Asp Phe Cys  
35 40 45

Pro Val Pro Tyr Cys Ser Gly Gly Arg His  
50 55

<210> 204  
<211> 75  
<212> PRT  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (66)  
<223> Xaa equals any one of the naturally occurring L-amino acids

<220>  
<221> misc feature  
<222> (73)  
<223> Xaa equals any one of the naturally occurring L-amino acids

<400> 204  
Met Lys Pro Thr Leu Ser Lys Phe Leu Gly Thr Asp Ala Glu Leu Pro  
1 5 10 15

Lys Leu Tyr Pro Pro Ser Leu Gln Ala Pro Arg Gly Glu Thr Gln Leu  
20 25 30

Leu Gly Pro Gly Leu Glu Arg Pro Thr Arg Glu Gly Arg Val Glu Gln  
35 40 45

Met Leu Phe Asn Gln Lys Ser Val Ser Trp Gly Ser Gln Leu Pro Gln  
50 55 60

Ser Xaa Asn Thr Phe Leu Lys Asn Xaa Asp Pro  
65 70 75



113

<210> 205  
 <211> 66  
 <212> PRT  
 <213> Homo sapiens  
  
 <220>  
 <221> misc feature  
 <222> (63)  
 <223> Xaa equals any one of the naturally occurring L-amino acids

<400> 205  
 Met Thr Trp Lys Gly Trp Ser Arg Thr Arg Ile Trp Lys Pro Ser Leu  
 1 5 10 15  
 Pro Gln Leu Phe Thr Met Tyr Leu Leu Ala Gln Ile Arg Ala Ala Ser  
 20 25 30  
 Arg Ala Ser Glu Asp Ser Cys Ser Tyr Ser Ser Asp Thr Met Trp Pro  
 35 40 45  
 Gln Ser Gly Asn Ser Ser Thr Phe Ala Phe Phe Arg Pro Arg Xaa Lys  
 50 55 60  
 Met Arg  
 65

<210> 206  
 <211> 44  
 <212> PRT  
 <213> Homo sapiens  
  
 <220>  
 <221> misc feature  
 <222> (44)  
 <223> Xaa equals stop translation

<400> 206  
 Met Leu Ser Phe Val Ser Arg Cys His Trp Ser Ser Ile Ala Glu Glu  
 1 5 10 15  
 Ser Glu Phe Leu Phe Leu Ile Leu Val Cys Tyr Phe Ser Ser Ser Cys  
 20 25 30  
 Ser Ser Cys Ile Ile His Gln Trp Tyr Tyr Val Xaa  
 35 40

<210> 207  
 <211> 32  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (32)  
 <223> Xaa equals stop translation

<400> 207  
 Met Leu Gln Thr Leu Ile Leu Ile Phe Leu Leu Leu Leu Pro Cys Tyr

114

1                    5                    10                    15  
 Leu Glu Leu Leu Cys Phe Ser Leu Ile Ser Ser Ser Ala Lys Thr Xaa  
                   20                    25                    30

&lt;210&gt; 208

&lt;211&gt; 48

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (11)

&lt;223&gt; Xaa equals any one of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (48)

&lt;223&gt; Xaa equals stop translation

&lt;400&gt; 208

Met Thr Pro Trp Leu Leu Ile Leu Val Ser Xaa Gly Phe Leu Lys Ser  
   1                    5                    10                    15

Ile Ser Asp Pro Gln Phe Gln Glu Leu Ser Ile Asn Ile Ala Ser Cys  
                   20                    25                    30

His Pro Gly Thr Val Met Pro Tyr Ser Gly Thr Ser His Leu Lys Xaa  
                   35                    40                    45

&lt;210&gt; 209

&lt;211&gt; 37

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (37)

&lt;223&gt; Xaa equals stop translation

&lt;400&gt; 209

Met Thr Gly Thr Pro Ala Trp Ala His Leu Leu Leu Leu Leu Leu  
   1                    5                    10                    15

Gly Ser Ala Pro Gln Thr Arg Leu Trp Pro Pro Ser Gln Cys Pro Val  
                   20                    25                    30

Thr Ser Pro Glu Xaa  
                   35

&lt;210&gt; 210

115

<211> 74  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (74)  
 <223> Xaa equals stop translation

<400> 210

Met	Gly	Val	Lys	Leu	Glu	Ile	Phe	Arg	Met	Ile	Ile	Tyr	Leu	Thr	Phe
1				5					10				15		
Pro	Val	Ala	Met	Phe	Trp	Val	Ser	Asn	Gln	Ala	Glu	Trp	Phe	Glu	Asp
			20					25					30		
Asp	Val	Ile	Gln	Arg	Lys	Arg	Glu	Leu	Trp	Pro	Pro	Glu	Lys	Leu	Gln
		35					40					45			
Glu	Ile	Glu	Glu	Phe	Lys	Glu	Arg	Leu	Arg	Lys	Arg	Arg	Glu	Glu	Lys
	50					55				60					
Leu	Leu	Arg	Asp	Ala	Gln	Gln	Asn	Ser	Xaa						
65						70									

<210> 211  
 <211> 41  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (41)  
 <223> Xaa equals stop translation

<400> 211

Met	Pro	Phe	Ser	Ser	Ser	Val	Lys	Cys	Leu	Phe	Gly	Val	Leu	Leu	Arg
1				5					10				15		
Phe	Cys	Phe	Val	Val	Phe	Ser	Val	Val	Val	Phe	Thr	Phe	Phe	Leu	Ser
			20					25					30		
Ile	Pro	Lys	Arg	Thr	Leu	Gly	Tyr	Xaa							
		35				40									

<210> 212  
 <211> 54  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (54)  
 <223> Xaa equals stop translation

<400> 212

Met	Trp	His	Leu	Ser	Phe	His	Cys	Leu	Leu	Leu	Leu	Pro	Leu	Cys
1				5				10				15		

Glu Val Thr His Ser Leu Phe Ala Phe Tyr His Asn Trp Lys Leu Phe  
20 25 30

Glu Ala Ser Leu Glu Thr Glu Ala Ala Met Leu Pro Val Gln Pro Ala  
35 40 45

Glu Pro Arg Ala Asn Xaa  
50

<210> 213

<211> 63

<212> PRT

<213> Homo sapiens

<220>

<221> misc feature

<222> (63)

<223> Xaa equals stop translation

<400> 213

Met Pro Glu Asn Leu Val Leu Ile Leu Ala Leu Leu Leu Ser Val Cys  
1 5 10 15

Gly Leu Lys Gln Val Ile Phe Leu Ser Ala Ser Ile Tyr Ser Lys Met  
20 25 30

Cys Thr Leu Ile Ala Thr Lys Lys Val Val Ala Lys Thr Arg Asn Asp  
35 40 45

Ala Tyr Trp Tyr Leu Ile Ser Leu Lys His Ile Val Gly Phe Xaa  
50 55 60

<210> 214

<211> 176

<212> PRT

<213> Homo sapiens

<220>

<221> misc feature

<222> (142)

<223> Xaa equals any one of the naturally occurring L-amino acids

<220>

<221> misc feature

<222> (149)

<223> Xaa equals any one of the naturally occurring L-amino acids

<220>

<221> misc feature

<222> (155)

<223> Xaa equals any one of the naturally occurring L-amino acids

<220>

<221> misc feature

<222> (158)

<223> Xaa equals any one of the naturally occurring L-amino acids

<220>  
 <221> misc feature  
 <222> (160)  
 <223> Xaa equals any one of the naturally occurring L-amino acids

<220>  
 <221> misc feature  
 <222> (163)  
 <223> Xaa equals any one of the naturally occurring L-amino acids

<220>  
 <221> misc feature  
 <222> (176)  
 <223> Xaa equals stop translation

<400> 214  
 Met Tyr Trp Ile Val Phe Ala Leu Tyr Thr Val Ile Glu Thr Val Ala  
           1                  5                  10                  15  
 Asp Gln Thr Val Ala Trp Phe Pro Leu Tyr Tyr Glu Leu Lys Ile Ala  
                   20                  25                  30  
 Phe Val Ile Trp Leu Leu Ser Pro Tyr Thr Lys Gly Ala Ser Leu Ile  
           35                  40                  45  
 Tyr Arg Lys Phe Leu His Pro Leu Leu Ser Ser Lys Glu Arg Glu Ile  
           50                  55                  60  
 Asp Asp Tyr Ile Val Gln Ala Lys Glu Arg Gly Tyr Glu Thr Met Val  
           65                  70                  75                  80  
 Asn Phe Gly Arg Gln Gly Leu Asn Leu Ala Ala Thr Ala Ala Val Thr  
                   85                  90                  95  
 Ala Ala Val Lys Ser Gln Gly Ala Ile Thr Glu Arg Leu Arg Ser Phe  
                   100                  105                  110  
 Ser Met His Asp Leu Thr Thr Ile Gln Gly Asp Glu Pro Val Gly Gln  
           115                  120                  125  
 Arg Pro Tyr Gln Pro Leu Pro Glu Ala Lys Lys Lys Ser Xaa Gln Pro  
           130                  135                  140  
 Pro Val Asn Gln Xaa Val Met Glu Phe His Xaa Lys Thr Xaa Met Xaa  
           145                  150                  155                  160  
 Lys Gln Xaa Lys Lys Gln Arg Gly His Ile Gln Ile Met Arg Cys Xaa  
                   165                  170                  175

<210> 215  
 <211> 40  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc feature

&lt;222&gt; (40)

&lt;223&gt; Xaa equals stop translation

&lt;400&gt; 215

Met Arg Glu Cys Tyr Phe Leu Gly Asn Phe Leu Leu Val Phe Leu Ile  
 1 5 10 15

Leu Ala Ser Ser Phe Ile Tyr Val Leu Val Thr Gln Val Leu Gly Gly  
 20 25 30

Pro Ala Thr Leu Leu Ala Phe Xaa  
 35 40

&lt;210&gt; 216

&lt;211&gt; 55

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (55)

&lt;223&gt; Xaa equals stop translation

&lt;400&gt; 216

Met Val Leu Gln Asn Thr Asn Thr Leu Leu Ile Val Ser Ala Phe Leu  
 1 5 10 15

Leu Ser Met Leu Phe Phe Lys Phe Ser Ile Ala Ile Phe Leu Val Thr  
 20 25 30

Asn Leu Ser Phe Glu Arg Ser Asn Leu Leu Leu Gly Pro Ser Ser Asp  
 35 40 45

Leu Phe Leu Asn Phe Lys Xaa  
 50 55

&lt;210&gt; 217

&lt;211&gt; 47

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (47)

&lt;223&gt; Xaa equals stop translation

&lt;400&gt; 217

Met Tyr Ile Phe His Phe Val Phe Leu Ile Gly Tyr Ala Met Cys Gly  
 1 5 10 15

Ile Gln Val Thr Asn Val Thr Leu Ala Ser Gly Pro Ser Asn Leu His  
 20 25 30

Val Tyr Leu Leu Gln Ser Tyr Leu Thr Arg Gly Pro Asn His Xaa  
 35 40 45

&lt;210&gt; 218

<211> 180  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (180)  
 <223> Xaa equals stop translation

<400> 218

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Met Leu Tyr Tyr Leu Trp Met Leu His Ser Val Thr Leu Phe Leu Asn
 1              5              10              15

Leu Leu Ala Cys Leu Ala Trp Phe Ser Gly Asn Ser Ser Lys Gly Val
      20              25              30

Asp Phe Gly Leu Ser Ile Leu Trp Phe Leu Ile Phe Thr Pro Cys Ala
      35              40              45

Phe Leu Cys Trp Tyr Arg Pro Ile Tyr Lys Ala Phe Arg Ser Asp Asn
      50              55              60

Ser Phe Ser Phe Phe Val Phe Phe Phe Val Phe Phe Cys Gln Ile Gly
      65              70              75              80

Ile Tyr Ile Ile Gln Leu Val Gly Ile Pro Gly Leu Gly Asp Ser Gly
      85              90              95

Trp Ile Ala Ala Leu Ser Thr Leu Asp Asn His Ser Leu Ala Ile Ser
      100             105             110

Val Ile Met Met Val Val Ala Gly Phe Phe Thr Leu Cys Ala Val Leu
      115             120             125

Ser Val Phe Leu Leu Gln Arg Val His Ser Leu Tyr Arg Arg Thr Gly
      130             135             140

Ala Ser Phe Gln Gln Ala Gln Glu Glu Phe Ser Gln Gly Ile Phe Ser
      145             150             155             160

Ser Arg Thr Phe His Arg Ala Ala Ser Ser Ala Ala Gln Gly Ala Phe
      165             170             175

Gln Gly Asn Xaa
      180

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<210> 219  
 <211> 99  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (99)  
 <223> Xaa equals stop translation

<400> 219

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Met Lys Leu Met Val Leu Val Phe Thr Ile Gly Leu Thr Leu Leu Leu
 1              5              10              15

```

120

Gly Val Gln Ala Met Pro Ala Asn Arg Leu Ser Cys Tyr Arg Lys Ile  
                   20                                  25                                  30  
 Leu Lys Asp His Asn Cys His Asn Leu Pro Glu Gly Val Ala Asp Leu  
                   35                                  40                                  45  
 Thr Gln Ile Asp Val Asn Val Gln Asp His Phe Trp Asp Gly Lys Gly  
                   50                                  55                                  60  
 Cys Glu Met Ile Cys Tyr Cys Asn Phe Ser Glu Leu Leu Cys Cys Pro  
                   65                                  70                                  75                                  80  
 Lys Asp Val Phe Phe Gly Pro Lys Ile Ser Phe Val Ile Pro Cys Asn  
                                   85                                  90                                  95  
 Asn Gln Xaa

<210> 220  
 <211> 44  
 <212> PRT  
 <213> Homo sapiens  
  
 <220>  
 <221> misc feature  
 <222> (44)  
 <223> Xaa equals stop translation

<400> 220  
 Met Gly Gly Lys Gly Ile Asn Tyr Thr Met Pro His Ile Cys Leu Leu  
   1                                  5                                  10                                  15  
 Leu Leu Asn Ala Leu Val Val Ser Cys Leu Leu Leu Glu Ala Ile Leu  
                   20                                  25                                  30  
 Leu Gln His Leu Val Leu Cys Asn Glu Leu Pro Xaa  
                   35                                  40

<210> 221  
 <211> 42  
 <212> PRT  
 <213> Homo sapiens  
  
 <220>  
 <221> misc feature  
 <222> (42)  
 <223> Xaa equals stop translation

<400> 221  
 Met Phe Met Leu Cys Asn Leu Leu Leu Pro Leu Leu Glu Phe Ile Phe  
   1                                  5                                  10                                  15  
 Gly Ser Thr Tyr Leu Ser Thr Asp Leu Tyr Leu His Thr Cys Met Lys  
                   20                                  25                                  30  
 Asn Val Phe Leu His Ile His Ser Phe Xaa  
                   35                                  40



121

<210> 222  
<211> 52  
<212> PRT  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (52)  
<223> Xaa equals stop translation

<400> 222  
Met Ala Val Pro Ser Gly Cys Trp Pro Ser Trp Pro Arg Pro Ser Ser  
1 5 10 15  
Trp Trp Ser Thr Arg Ile Ser Pro Arg Ser Ala Thr Pro Leu Thr Ala  
20 25 30  
Ser Thr Trp Ser Leu Val Thr Cys Ser Ser Gln Val Ser Ala Cys Gly  
35 40 45  
Thr Ser Ile Xaa  
50

<210> 223  
<211> 32  
<212> PRT  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (32)  
<223> Xaa equals stop translation

<400> 223  
Met Val Ser Leu Asn Leu Ser Leu Pro Asn Asn Ile Ile Ser Leu Val  
1 5 10 15  
Phe Phe Phe Leu Leu Gln Pro Val Gln Lys Gly Val Ser Gly Gly Xaa  
20 25 30

<210> 224  
<211> 54  
<212> PRT  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (54)  
<223> Xaa equals stop translation

<400> 224  
Met Leu Val Leu Met Thr Thr Cys Ile Leu Ala Ala Val Cys Val His  
1 5 10 15

122

Thr Ala Gln Cys Ala Pro Asp Ser Arg Met Asp Asn Asp Cys Pro Ser  
                   20                                  25                                  30

His Gln Ala Gln Ile His Phe Arg Ala Ser Glu Val Arg Arg Gly Trp  
                   35                                  40                                  45

Thr Phe Asn His Asp Xaa  
                   50

&lt;210&gt; 225

&lt;211&gt; 41

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (41)

&lt;223&gt; Xaa equals stop translation

&lt;400&gt; 225

Met Gly Pro Ser Gln Arg Glu Val Thr Val Gln Trp His Arg Ala Leu  
       1                                  5                                  10                                  15

Phe Leu Leu Pro Leu Leu Leu Leu Ser Thr Arg Thr Glu Thr Lys Asn  
                   20                                  25                                  30

Phe Gly Phe Lys Trp Leu Lys Asp Xaa  
           35                                  40

&lt;210&gt; 226

&lt;211&gt; 31

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (31)

&lt;223&gt; Xaa equals stop translation

&lt;400&gt; 226

Met Gln Leu Ser Lys Phe Leu Leu Phe Leu Phe Val Tyr Thr Arg Glu  
       1                                  5                                  10                                  15

Asn Pro Thr Ser Ala Cys Val Trp Gly Glu Lys Ser Thr Val Xaa  
                   20                                  25                                  30

&lt;210&gt; 227

&lt;211&gt; 60

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (60)

&lt;223&gt; Xaa equals stop translation

123

&lt;400&gt; 227

Met Val Val Val Ser Thr Asn Gly Phe Leu Leu Leu Leu Leu Phe Leu  
1 5 10 15

Asn Arg Lys Ser Gly Leu Cys Ser Tyr Arg Lys Ala Val His Arg Leu  
20 25 30

Ser Ser Cys Pro Ser Arg His Gln Ala Gly Pro Arg Ile Lys Cys Asp  
35 40 45

Phe Lys Trp Gly Lys Leu Cys Tyr Ser Cys Ala Xaa  
50 55 60

&lt;210&gt; 228

&lt;211&gt; 35

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (35)

&lt;223&gt; Xaa equals stop translation

&lt;400&gt; 228

Met Gly Trp Gly Lys Glu Val Val Ser Leu Ile Val Leu Leu Val Asn  
1 5 10 15

Leu Phe Leu Cys Pro Trp Ala Leu Gly Leu Cys Leu Leu Ser Val Ser  
20 25 30

Ser Leu Xaa  
35

&lt;210&gt; 229

&lt;211&gt; 39

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (39)

&lt;223&gt; Xaa equals stop translation

&lt;400&gt; 229

Met Met Asn Ile Leu Leu Leu Lys Tyr Ile Leu Glu Ile Leu Ile Leu  
1 5 10 15

Ser Glu Asn Leu Asn Leu Phe Asn Ile Thr Tyr Gly Lys Tyr Asn Leu  
20 25 30

Phe Phe Leu Tyr Arg Tyr Xaa  
35

&lt;210&gt; 230

&lt;211&gt; 39

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

124

<220>  
 <221> misc feature  
 <222> (39)  
 <223> Xaa equals stop translation

<400> 230  
 Met Tyr Ile Phe Tyr Leu Tyr Lys Ile Tyr Ile Tyr Thr His Ile Cys  
     1                    5                    10                    15  
 Ile Tyr Ile Pro Leu Phe Leu Cys Leu Leu Ile Leu Ala Ile Lys Glu  
                     20                    25                    30  
 Gly Ala Ala Phe Asn Val Xaa  
                     35

<210> 231  
 <211> 62  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (62)  
 <223> Xaa equals stop translation

<400> 231  
 Met Asn Glu Ser Val Tyr Asp Asp Ser Thr Ser Ser Tyr Thr Pro Ser  
     1                    5                    10                    15  
 Leu His Ile Leu Gly Cys Leu Leu Leu Leu Phe Leu Gly Val Glu Arg  
                     20                    25                    30  
 Ala Leu Glu Pro Phe Ser Gly Leu Cys Ala Ser Leu His Asp Val Arg  
                     35                    40                    45  
 Pro Ile Val Asn Pro Leu Thr Ser Phe Ser Leu Ile Tyr Xaa  
                     50                    55                    60

<210> 232  
 <211> 198  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (198)  
 <223> Xaa equals stop translation

<400> 232  
 Met Cys Thr Gly Lys Cys Ala Arg Cys Val Gly Leu Ser Leu Ile Thr  
     1                    5                    10                    15  
 Leu Cys Leu Val Cys Ile Val Ala Asn Ala Leu Leu Leu Val Pro Asn  
                     20                    25                    30  
 Gly Glu Thr Ser Trp Thr Asn Thr Asn His Leu Ser Leu Gln Val Trp  
                     35                    40                    45

125

Leu Met Gly Gly Phe Ile Gly Gly Gly Leu Met Val Leu Cys Pro Gly  
 50 55 60  
 Ile Ala Ala Val Arg Ala Gly Gly Lys Gly Cys Cys Gly Ala Gly Cys  
 65 70 75 80  
 Cys Gly Asn Arg Cys Arg Met Leu Arg Ser Val Phe Ser Ser Ala Phe  
 85 90 95  
 Gly Val Leu Gly Ala Ile Tyr Cys Leu Ser Val Ser Gly Ala Gly Leu  
 100 105 110  
 Arg Asn Gly Pro Arg Cys Leu Met Asn Gly Glu Trp Gly Tyr His Phe  
 115 120 125  
 Glu Asp Thr Ala Gly Ala Tyr Leu Leu Asn Arg Thr Leu Trp Asp Arg  
 130 135 140  
 Cys Glu Ala Pro Pro Arg Val Val Pro Trp Asn Val Thr Leu Phe Ser  
 145 150 155 160  
 Leu Leu Val Ala Ala Ser Cys Leu Glu Ile Val Leu Cys Gly Ile Gln  
 165 170 175  
 Leu Val Asn Ala Thr Ile Gly Val Phe Cys Gly Asp Cys Arg Lys Lys  
 180 185 190  
 Gln Asp Thr Pro His Xaa  
 195

<210> 233  
 <211> 62  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (62)  
 <223> Xaa equals stop translation

<400> 233  
 Met Ser Gln Leu Phe Leu Ile Met Leu Thr Phe Ile Phe Leu Asn Asn  
 1 5 10 15  
 Met Phe Ile Met His Leu Thr Ser Phe His Gly Lys Arg Val Phe Gly  
 20 25 30  
 Phe Leu Asn Gln Ser Ser His Met His Ala Phe Pro Leu Pro Arg Trp  
 35 40 45  
 Thr Thr Ser Ile Phe Ser Val Ser Ile Phe Ile Asn Arg Xaa  
 50 55 60

<210> 234  
 <211> 81  
 <212> PRT  
 <213> Homo sapiens

126

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (81)

&lt;223&gt; Xaa equals stop translation

&lt;400&gt; 234

Met Ala Phe Leu Pro Leu Thr Leu Thr Phe Cys Leu Ala Pro Leu Ala  
1 5 10 15

Pro Leu Leu Pro Ser Ile Trp Gly Pro Thr Pro Ala Ser Cys Val Val  
20 25 30

Trp Pro Leu Leu Thr Ile Leu Pro Val Pro Ala Gln Ala Ser Pro Ser  
35 40 45

Thr Asp Thr Ala His Leu Trp Gln Arg Pro Thr Thr Gly Ser Pro Thr  
50 55 60

Arg Leu Val Arg Pro Leu Pro Arg Pro Gly Leu Pro Pro Met Trp Ala  
65 70 75 80

Xaa

&lt;210&gt; 235

&lt;211&gt; 111

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 235

Met Gly Gly Leu Glu Pro Cys Ser Arg Leu Leu Leu Pro Leu Leu  
1 5 10 15

Leu Ala Val Gly Leu Arg Pro Val Gln Ala Gln Ala Gln Ser Asp Cys  
20 25 30

Ser Cys Ser Thr Val Ser Pro Gly Val Leu Ala Gly Ile Val Met Gly  
35 40 45

Asp Leu Val Leu Thr Val Leu Ile Ala Leu Ala Val Tyr Phe Leu Gly  
50 55 60

Arg Leu Val Pro Arg Gly Arg Gly Ala Ala Glu Ala Thr Arg Lys Gln  
65 70 75 80

Arg Ile Thr Glu Thr Glu Ser Pro Tyr Gln Glu Leu Gln Gly Gln Arg  
85 90 95

Ser Asp Val Tyr Ser Asp Leu Asn Thr Gln Arg Pro Tyr Tyr Lys  
100 105 110

&lt;210&gt; 236

&lt;211&gt; 33

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

127

&lt;221&gt; misc feature

&lt;222&gt; (33)

&lt;223&gt; Xaa equals stop translation

&lt;400&gt; 236

Met Gln Arg Met Leu Val Leu Leu Phe Phe Phe Ser Leu Leu Ala  
 1 5 10 15

Ile Asn Pro Ala Glu Thr Ile Cys Gly Tyr Gly Ser Thr Trp Lys Phe  
 20 25 30

Xaa

&lt;210&gt; 237

&lt;211&gt; 229

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (134)

&lt;223&gt; Xaa equals any one of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (229)

&lt;223&gt; Xaa equals stop translation

&lt;400&gt; 237

Met Val Leu Gly Leu Phe Val Pro Pro Val Phe Val Val Ser Tyr Ala  
 1 5 10 15

Lys Asp Leu Gly Val Pro Asp Thr Lys Ala Ala Phe Leu Leu Thr Ile  
 20 25 30

Leu Gly Phe Ile Asp Ile Phe Ala Arg Pro Ala Ala Gly Phe Val Ala  
 35 40 45

Gly Leu Gly Lys Val Arg Pro Tyr Ser Val Tyr Leu Phe Ser Phe Ser  
 50 55 60

Met Phe Phe Asn Gly Leu Ala Asp Leu Ala Gly Ser Thr Ala Gly Asp  
 65 70 75 80

Tyr Gly Gly Leu Val Val Phe Cys Ile Phe Phe Gly Ile Ser Tyr Gly  
 85 90 95

Met Val Gly Ala Leu Gln Phe Glu Val Leu Met Ala Ile Val Gly Thr  
 100 105 110

His Lys Phe Ser Ser Ala Ile Gly Leu Val Leu Leu Met Glu Ala Val  
 115 120 125

Ala Val Leu Val Gly Xaa Pro Ser Gly Gly Lys Leu Leu Asp Ala Thr  
 130 135 140

His Val Tyr Met Tyr Val Phe Ile Leu Ala Gly Ala Glu Val Leu Thr  
 145 150 155 160

128

Ser Ser Leu Ile Leu Leu Leu Gly Asn Phe Phe Cys Ile Arg Lys Lys  
 165 170 175

Pro Lys Glu Pro Gln Pro Glu Val Ala Ala Glu Glu Lys Leu  
 180 185 190

His Lys Pro Pro Ala Asp Ser Gly Val Asp Leu Arg Glu Val Glu His  
 195 200 205

Phe Leu Lys Ala Glu Pro Glu Lys Asn Gly Glu Val Val His Thr Pro  
 210 215 220

Glu Thr Ser Val Xaa  
 225

<210> 238

<211> 117

<212> PRT

<213> Homo sapiens

<220>

<221> misc feature

<222> (117)

<223> Xaa equals stop translation

<400> 238

Met Thr Pro Leu Leu Thr Leu Ile Leu Val Val Leu Met Gly Leu Pro  
 1 5 10 15

Leu Ala Gln Ala Leu Asp Cys His Val Cys Ala Tyr Asn Gly Asp Asn  
 20 25 30

Cys Phe Asn Pro Met Arg Cys Pro Ala Met Val Ala Tyr Cys Met Thr  
 35 40 45

Thr Arg Thr Tyr Tyr Thr Pro Thr Arg Met Lys Val Ser Lys Ser Cys  
 50 55 60

Val Pro Arg Cys Phe Glu Thr Val Tyr Asp Gly Tyr Ser Lys His Ala  
 65 70 75 80

Ser Thr Thr Ser Cys Cys Gln Tyr Asp Leu Cys Asn Gly Thr Gly Leu  
 85 90 95

Ala Thr Pro Ala Thr Leu Ala Leu Ala Pro Ile Leu Leu Ala Thr Leu  
 100 105 110

Trp Gly Leu Leu Xaa  
 115

<210> 239

<211> 37

<212> PRT

<213> Homo sapiens

<220>

<221> misc feature



&lt;222&gt; (37)

&lt;223&gt; Xaa equals stop translation

&lt;400&gt; 239

Met Leu Thr Trp Leu Asp Leu Asp Leu Leu Phe Cys Phe Leu Phe Leu  
1 5 10 15

Phe Leu Phe Ile Leu Phe Tyr Phe Leu Gln Leu Asn Glu Phe Trp Gly  
20 25 30

Gly Asn Pro Phe Xaa  
35

&lt;210&gt; 240

&lt;211&gt; 39

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (39)

&lt;223&gt; Xaa equals stop translation

&lt;400&gt; 240

Ser Leu Gly Val Gly Phe Phe Phe Phe Phe Ser Ser Leu Lys Glu  
1 5 10 15

Pro Ala Val Ala Leu Cys Val Phe Cys Phe Cys Phe Pro Phe Gly Gly  
20 25 30

Pro Met Gly Lys Ser Phe Xaa  
35

&lt;210&gt; 241

&lt;211&gt; 48

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (48)

&lt;223&gt; Xaa equals stop translation

&lt;400&gt; 241

Met Gln Ser Gly Arg Ser Trp Ala Leu Lys Met Val Leu Leu Cys Asn  
1 5 10 15

Ser Cys Leu Gly Leu Gly Val Gly Ser Val Gly Pro Ser Met Ser Ser  
20 25 30

Leu Phe Gly Ala Val Leu Ser Glu Thr Pro Gly Ser Ser Val Tyr Xaa  
35 40 45

&lt;210&gt; 242

130

<211> 32  
<212> PRT  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (32)  
<223> Xaa equals stop translation

<400> 242  
Met Ile Thr Leu Cys Ile Phe Leu Leu Phe Lys Val Phe Val Gly Ile  
1 5 10 15  
Ile Leu His Tyr Leu Ile Gly Lys Asn Ile Tyr Val Tyr Ser Val Xaa  
20 25 30

<210> 243  
<211> 64  
<212> PRT  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (64)  
<223> Xaa equals stop translation

<400> 243  
Met Ala Ser Leu Leu Gln Arg Asn Leu Cys Pro Arg Leu Ser Val Cys  
1 5 10 15  
Leu Val Phe Ile Gln Val Phe Val Cys Cys Val Glu Gly Gly Gly Arg  
20 25 30  
Arg Val Lys Ala Val Leu Phe Arg Ala Pro Phe Gly Glu His Ser Arg  
35 40 45  
Gln Asn Thr Leu Val Ile Pro Ser Gln Thr Gly Leu Gln Ala His Xaa  
50 55 60

<210> 244  
<211> 68  
<212> PRT  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (68)  
<223> Xaa equals stop translation

<400> 244  
Met Pro Val Tyr Asp Phe Asn Trp Trp Tyr Ser Leu Tyr Phe Ile Ile  
1 5 10 15

131

Tyr Ile Ile Ile Asn Thr Tyr Ile Phe Lys Ser Val Phe Leu Ala Met  
                   20                  25                  30

Val Tyr Ser Asn Tyr Arg Lys His Phe His Ile Leu Cys Val Cys Val  
           35                  40                  45

Cys Val Phe Cys Ser Asp Glu Gln Asn Leu Leu Phe Thr Gln Phe Tyr  
       50                  55                  60

Tyr Leu Ser Xaa  
       65

<210> 245

<211> 46

<212> PRT

<213> Homo sapiens

<220>

<221> misc feature

<222> (43)

<223> Xaa equals any one of the naturally occurring L-amino acids

<220>

<221> misc feature

<222> (46)

<223> Xaa equals stop translation

<400> 245

Met Ser Asp Lys Leu Ser Pro Ser Thr Val Pro Leu Leu Leu Pro Val  
       1                  5                  10                  15

Leu Phe Lys Val Thr Ile Leu Leu Gln Arg Val Cys Pro Glu Asp Ser  
           20                  25                  30

Pro Ser Ser Ser Val Leu Pro Glu Ser Val Xaa Arg Glu Xaa  
           35                  40                  45

<210> 246

<211> 43

<212> PRT

<213> Homo sapiens

<220>

<221> misc feature

<222> (43)

<223> Xaa equals stop translation

<400> 246

Met Arg Lys Glu Glu Gly Ile Ala His Leu Ser Ile Ala Phe Phe Val  
       1                  5                  10                  15

Gln Val Leu Cys Leu Tyr Gln Leu Leu Pro Val Ile Leu Pro Gln Phe  
           20                  25                  30

Asn Leu Gly Ser Gly Lys Asn Met Asn Arg Xaa  
       35                  40

<210> 247  
<211> 32  
<212> PRT  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (11)  
<223> Xaa equals any one of the naturally occurring L-amino acids

<220>  
<221> misc feature  
<222> (32)  
<223> Xaa equals stop translation

<400> 247  
Met Ile His Val Leu Thr Phe Leu Leu Gln Xaa Tyr Ile Leu Ile Ser  
1 5 10 15  
Lys Gly Lys Gly Asp Val Ser Gln Phe Val Lys Ser Arg Glu Tyr Xaa  
20 25 30

<210> 248  
<211> 24  
<212> PRT  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (24)  
<223> Xaa equals stop translation

<400> 248  
Met Ser Glu Leu Ser Ala Phe Met Phe Ser Thr Ile Ile Phe Leu Met  
1 5 10 15  
Ala Gln Pro Thr Ser Cys Phe Xaa  
20

<210> 249  
<211> 80  
<212> PRT  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (36)  
<223> Xaa equals any one of the naturally occurring L-amino acids

<220>  
<221> misc feature  
<222> (80)  
<223> Xaa equals stop translation

133

&lt;400&gt; 249

Met Arg Val Phe Ala Leu Leu Pro Pro Phe His Lys Ser Thr Val Leu  
 1 5 10 15

Ser Phe Leu Leu Phe Phe Leu Ser Phe Phe Phe Arg Gln Gly Leu  
 20 25 30

Ala Val Ser Xaa Arg Leu Glu Cys Ser Gly Ala Ile Ile Ala His Cys  
 35 40 45

Ser Leu Asp Leu Leu Asp Ser Ser Asn Pro Pro Ala Leu Thr Ser Gln  
 50 55 60

Leu Leu Arg Arg Pro Arg Gln Glu Asp His Leu Ser Pro Gly Gly Xaa  
 65 70 75 80

&lt;210&gt; 250

&lt;211&gt; 16

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (16)

&lt;223&gt; Xaa equals stop translation

&lt;400&gt; 250

Met Ser His Cys Ala Trp Leu His Leu Gln Leu Phe Leu Ser Leu Xaa  
 1 5 10 15

&lt;210&gt; 251

&lt;211&gt; 47

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (47)

&lt;223&gt; Xaa equals stop translation

&lt;400&gt; 251

Met Met Phe Cys Phe Leu Ile Trp Val Val Val Thr Phe Thr Tyr Ser  
 1 5 10 15

Leu Asn Cys Thr Phe Val Leu His Lys Phe Ile Ile Phe Pro Asn Phe  
 20 25 30

Lys Lys Val Lys Arg Arg Arg Lys Lys Leu Val Met Lys Val Xaa  
 35 40 45

&lt;210&gt; 252

<211> 32  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (32)  
 <223> Xaa equals stop translation

<400> 252  
 Met Pro Pro Pro Glu Cys Leu Ser Asp Cys Ser Lys Val Ala Leu Val  
           1                  5                  10                  15  
 Met Val Leu Phe Leu Phe Leu His Gln Ser Ser Cys Trp Ala Ala Xaa  
                   20                  25                  30

<210> 253  
 <211> 36  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (36)  
 <223> Xaa equals stop translation

<400> 253  
 Met Ala Ser Ser Val Thr Val Lys Glu Val Cys Val Leu Phe Asn Leu  
           1                  5                  10                  15  
 Leu Ile Ile Ile Thr Ala Met Val Tyr His Ser Phe Thr Lys Tyr Gln  
                   20                  25                  30  
 Thr Leu Phe Xaa  
                   35

<210> 254  
 <211> 51  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (51)  
 <223> Xaa equals stop translation

<400> 254  
 Met Ile Phe Leu Phe Phe Ile Leu Phe Glu Ile Ile Val Thr Leu Trp  
           1                  5                  10                  15  
 Leu Thr Pro Thr Tyr Pro Gln Ala Phe Ser Glu Leu Thr Ile Gln Ile  
                   20                  25                  30  
 Thr Ala Pro Phe Gly Ser Leu Pro Gln Gln Leu Tyr Leu His Met Ser  
           35                  40                  45

Ile Ile Xaa  
50

<210> 255  
<211> 76  
<212> PRT  
<213> Homo sapiens

<400> 255  
Met Phe Phe Leu Leu Ile Leu Cys Trp Leu Leu Cys Leu Ser Leu Ser  
1 5 10 15  
Gly Leu Tyr Pro Arg Leu Leu Asn Pro Gly Gly Trp Leu Ser Leu Leu  
20 25 30  
Ser Phe Gln Met Asp Tyr Gly Trp Ile Leu Pro Trp Gly Ala Cys Thr  
35 40 45  
Val Arg His Gly Lys Pro Gly Met Gly Lys Arg Ser Gly Gly Ser Leu  
50 55 60  
Pro His Leu Thr Ala Leu Val Leu Cys Leu Thr Ser  
65 70 75

<210> 256  
<211> 61  
<212> PRT  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (61)  
<223> Xaa equals stop translation

<400> 256  
Met Leu Leu Ser Asn Leu Ser Leu Ser Leu Gln Pro Leu Leu Phe Leu  
1 5 10 15  
Phe Ser Phe Phe Leu Phe Cys Lys Met Gly Ser Arg Lys Gly Leu Arg  
20 25 30  
His Lys Thr Gln His Phe Ser Ser Met Thr Asp Gln Ile Leu Lys Gly  
35 40 45  
Ser Val Arg Ser Pro Ala Leu Gly Gln Leu His Asp Xaa  
50 55 60

<210> 257  
<211> 37  
<212> PRT  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (37)  
<223> Xaa equals stop translation

&lt;400&gt; 257

Met Tyr Glu Val Asp Lys Lys Ile Tyr Ser Asn Phe Ile Gln Ile Leu  
1 5 10 15

Ile Val Ile Ile Phe Val Leu Tyr Leu Ile Ile Asn Gln Asn Thr Phe  
20 25 30

Ala Phe Leu Ser Xaa  
35

&lt;210&gt; 258

&lt;211&gt; 43

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (43)

&lt;223&gt; Xaa equals stop translation

&lt;400&gt; 258

Met Cys Ile Leu Pro Leu Met Leu Thr Tyr Pro Ile Leu Pro Lys Val  
1 5 10 15

Val Gly Asn Asn Ile Leu Leu Gly Asp Ser Gly Leu Thr Ser Leu Val  
20 25 30

Ile Pro Leu Ser Val Val Phe Asn Leu Lys Xaa  
35 40

&lt;210&gt; 259

&lt;211&gt; 39

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (39)

&lt;223&gt; Xaa equals stop translation

&lt;400&gt; 259

Met Ile Leu Val Ser Lys Leu Phe Phe Gly Phe Ser Leu Met Phe Leu  
1 5 10 15

Ile Phe Phe Pro Leu Ala Thr Met Thr Val His Val Leu Ile Asn Ile  
20 25 30

Gly Arg Ser Arg Tyr Lys Xaa  
35

&lt;210&gt; 260

&lt;211&gt; 51

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;



<221> misc feature

<222> (51)

<223> Xaa equals stop translation

<400> 260

Met Ser Ile Thr Ser Asn Thr Tyr Phe Phe Leu Leu Gly Ala Phe Lys  
1 5 10 15

Ile Leu Ser Ser Ser Tyr Trp Lys Ile His Thr Lys Leu Leu Leu Thr  
20 25 30

Ile Val Pro Leu Gln Cys Cys Gly Met Pro Gln Leu Ile Pro Pro Leu  
35 40 45

Gln Leu Xaa  
50

<210> 261

<211> 76

<212> PRT

<213> Homo sapiens

<220>

<221> misc feature

<222> (76)

<223> Xaa equals stop translation

<400> 261

Met Phe Thr Thr Arg Phe Pro Lys Leu Leu Ile Phe Pro Lys Ile Val  
1 5 10 15

Thr Glu Asn Cys Cys Leu Leu Phe Cys Ser Phe Trp Gly Trp Trp Cys  
20 25 30

Trp Leu Gly His Ala Cys Glu Val Met Cys Val Ser Asp Leu Thr Asp  
35 40 45

Ser Leu Phe Ser Leu Leu Ile Glu Arg Ala Leu Phe Thr Leu Phe Ile  
50 55 60

Cys Phe Asp Thr Ser Ala Phe Ser Val Leu Ser Xaa  
65 70 75

<210> 262

<211> 45

<212> PRT

<213> Homo sapiens

<220>

<221> misc feature

<222> (45)

<223> Xaa equals stop translation

<400> 262

Met Thr Ser His Pro Ser Trp Arg Leu Ile Leu Val Thr Ser Leu Val  
1 5 10 15

Leu Gly Val Glu Pro Glu Glu Ala Pro Gly Glu Ala Gly Glu Gly Ser

138

20                      25                      30  
 Gly Gly Gln Arg Thr Met Asp Pro Glu Gln Lys Trp Xaa  
          35                      40                      45

<210> 263  
 <211> 53  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (53)  
 <223> Xaa equals stop translation

<400> 263  
 Met Pro Ser Leu Asn Leu Val Leu Arg Pro Leu Ile Cys Leu Ala Ser  
      1                      5                      10                      15

Ile Thr Ser Phe Leu Ile Phe Phe Pro Leu Leu Thr Leu Ile Leu Cys  
          20                      25                      30

Ser Pro Asn Ser Pro Pro Phe Pro Leu Pro Ala His Pro Glu Arg His  
          35                      40                      45

Thr His Thr Gln Xaa  
      50

<210> 264  
 <211> 43  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (43)  
 <223> Xaa equals stop translation

<400> 264  
 Met His Ala Leu Ser Tyr Thr His Leu Ser Leu Leu Ser Leu Phe Leu  
      1                      5                      10                      15

Phe Leu Pro Pro Ser Phe Leu Tyr Tyr Asn Leu Val Ile Leu Phe Phe  
          20                      25                      30

Glu Ala Phe Gln Asn Ile Ser His Leu Ser Xaa  
          35                      40

<210> 265  
 <211> 50  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (50)  
 <223> Xaa equals stop translation

&lt;400&gt; 265

Asp Trp Leu Leu Leu Ser Met Thr Phe Leu Gly Leu Ala Thr Gln  
1 5 10 15

Leu Val Ser Val Val His Ser Phe Cys Ser Arg Ile Val Phe Cys Cys  
20 25 30

Leu Asp Gly Pro Pro Val Cys Cys Leu Phe Thr Leu Gln Leu Val Asp  
35 40 45

Ile Xaa

50

&lt;210&gt; 266

&lt;211&gt; 52

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (52)

&lt;223&gt; Xaa equals stop translation

&lt;400&gt; 266

Met Arg Lys Ser Gly Ala Met Lys Lys Gly Gly Ile Phe Ser Ala Glu  
1 5 10 15

Phe Leu Lys Val Phe Ile Pro Ser Leu Phe Leu Ser His Val Leu Ala  
20 25 30

Leu Gly Leu Gly Ile Tyr Ile Gly Lys Arg Leu Ser Thr Pro Ser Ala  
35 40 45

Ser Thr Tyr Xaa

50

&lt;210&gt; 267

&lt;211&gt; 41

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (41)

&lt;223&gt; Xaa equals stop translation

&lt;400&gt; 267

Met Trp Val Gln Leu Ile Phe Phe Phe Val Gln Tyr Gly Asp Ser Leu  
1 5 10 15

Thr Ser Ala Phe Phe Pro Phe Ser Ser Asn Phe Ser Leu Gln Asn Ser  
20 25 30

Gly Phe Ser Met His Lys Leu Lys Xaa  
35 40

140

&lt;210&gt; 268

&lt;211&gt; 79

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (79)

&lt;223&gt; Xaa equals stop translation

&lt;400&gt; 268

Met Val Cys Phe Gln Ser Asn Lys Pro Ser Thr Ser Thr Trp Arg Gln

1 5 10 15

Leu Ser Phe Val Phe Val Leu Phe Cys Leu Phe Cys Leu Gly His Ala

20 25 30

Phe Leu Ser Leu Pro Phe Tyr Ile Leu Ser Ile Ile Ala Met Cys Leu

35 40 45

Glu Gln Trp Ala Phe His Asn Met Asn Ser Leu Tyr His His Glu Trp

50 55 60

Glu Val Arg Gly Asn Leu Ile His Val Asp Phe Thr Leu Pro Xaa

65 70 75

&lt;210&gt; 269

&lt;211&gt; 117

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (117)

&lt;223&gt; Xaa equals stop translation

&lt;400&gt; 269

Met Thr His Lys Ser Leu Val Tyr Leu Trp Phe Leu Cys Ser Ser Val

1 5 10 15

Ala Leu Ala Leu Gly Ala Leu Thr Val Trp His Ala Val Leu Ile Ser

20 25 30

Arg Gly Glu Thr Ser Ile Glu Arg His Ile Asn Lys Lys Glu Arg Arg

35 40 45

Arg Leu Gln Ala Lys Gly Arg Val Phe Arg Asn Pro Tyr Asn Tyr Gly

50 55 60

Cys Leu Asp Asn Trp Lys Val Phe Leu Gly Val Asp Thr Gly Arg His

65 70 75 80

Trp Leu Thr Arg Val Leu Leu Pro Ser Ser His Leu Pro His Gly Asn

85 90 95

Gly Met Ser Trp Glu Pro Pro Pro Trp Val Thr Ala His Ser Ala Ser

100 105 110

Val Met Ala Val Xaa

141

115

&lt;210&gt; 270

&lt;211&gt; 62

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (62)

&lt;223&gt; Xaa equals stop translation

&lt;400&gt; 270

Met Ser Asn Leu Gln Phe His Leu Leu Pro His Ser Ser Pro Ile Leu  
 1 5 10 15

Pro Leu Phe Thr Leu Ala Leu Leu Lys Met Gln Ile Pro Gly Leu Arg  
 20 25 30

Leu Ser His Cys Leu Leu Thr Tyr Asn Ser Tyr Thr Arg Thr Pro Phe  
 35 40 45

Leu Leu Pro Ser Ser Glu Ser Tyr Leu Val Phe Glu Ile Xaa  
 50 55 60

&lt;210&gt; 271

&lt;211&gt; 98

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (53)

&lt;223&gt; Xaa equals any one of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (56)

&lt;223&gt; Xaa equals any one of the naturally occurring L-amino acids

&lt;400&gt; 271

Met Leu Pro Leu Tyr Phe Leu Gln Pro Tyr Leu Ser Leu Val Ile Phe  
 1 5 10 15

Ile Met Leu Arg Asp Asn Trp His Leu Leu Ala Leu Thr Cys Ser Tyr  
 20 25 30

Ser Ile Ile Trp Arg Leu Ser Pro Asp Thr Asn Pro Ser Pro Ile Ala  
 35 40 45

Pro Ser Arg His Xaa Gln Leu Xaa Val Val Ala Ile Ala Pro Leu Glu  
 50 55 60

Pro Ser Pro His Ser His Met Gln Ser Ile Pro Lys Asn Leu Ala Gln  
 65 70 75 80

Phe Ser Ser Ser Gln Met Phe Ser Leu Thr Leu Gln Leu Val Tyr Ile  
 85 90 95

Ser Ser

<210> 272

<211> 32

<212> PRT

<213> Homo sapiens

<220>

<221> misc feature

<222> (32)

<223> Xaa equals stop translation

<400> 272

Met	Tyr	Ile	Leu	Ser	Leu	Ser	Cys	Ser	Ile	Phe	Phe	Ser	Phe	Phe	Phe
1				5					10					15	

Phe	Leu	Phe	Pro	Phe	Phe	Arg	Gly	Leu	Arg	Lys	Gly	Gln	Ala	Lys	Xaa
			20					25					30		

<210> 273

<211> 15

<212> PRT

<213> Homo sapiens

<220>

<221> misc feature

<222> (15)

<223> Xaa equals stop translation

<400> 273

Ala	Ser	Ser	Leu	Leu	Val	Ser	Leu	Gln	Cys	Leu	Leu	Gln	Leu	Xaa
1				5				10					15	

<210> 274

<211> 37

<212> PRT

<213> Homo sapiens

<220>

<221> misc feature

<222> (37)

<223> Xaa equals stop translation

<400> 274

Met	Cys	Phe	Ile	Leu	Val	Val	Cys	Phe	Ala	Ser	Leu	Ile	Thr	Glu	Cys
1				5					10					15	

Pro	Cys	His	Cys	Lys	Cys	Cys	Arg	Asp	Val	Gly	Arg	Gly	Pro	Thr	Val
			20				25						30		

Leu	Tyr	Glu	Met	Xaa
			35	

<210> 275  
<211> 57  
<212> PRT  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (53)  
<223> Xaa equals any one of the naturally occurring L-amino acids

<220>  
<221> misc feature  
<222> (57)  
<223> Xaa equals stop translation

<400> 275  
Met His Arg Leu Trp Ile Gly Pro Ala Phe Phe Leu Met Thr Ser Leu  
1 5 10 15  
Ser Val Ser Gly Ala Val Ile Pro Arg Asn Gly Gly Pro Gly Gly Val  
20 25 30  
Ser Ser Gly Pro Cys Leu Leu Gln Leu Leu Cys Gly Gln Ala Gly Ser  
35 40 45  
Ser Thr Ile Arg Xaa Ile Pro Ser Xaa  
50 55

<210> 276  
<211> 27  
<212> PRT  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (27)  
<223> Xaa equals stop translation

<400> 276  
Met Glu Ala Val Phe Phe Leu Phe Phe Leu Leu Leu Leu Thr Trp  
1 5 10 15  
Thr Ser Lys Ile Ala Pro Ile Leu Phe Ser Xaa  
20 25

<210> 277  
<211> 68  
<212> PRT  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (68)  
<223> Xaa equals stop translation

<400> 277

Asp Trp Gly Phe Gln Thr Thr Phe Phe Ser Leu Gly Leu Tyr Leu Phe  
 1 5 10 15  
 Thr Ile Trp Trp Ser Thr Val Gly Leu Pro Trp Thr Ser Ser Thr Gln  
 20 25 30  
 Arg Glu Leu Asp Met Lys Leu Glu Ala Ala Ala Leu Glu Gly Lys Phe  
 35 40 45  
 Arg Leu Thr Trp Thr Ala Gln Ala Met Ala Gly Arg Ile Pro Ser Ser  
 50 55 60  
 Trp Gly Pro Xaa  
 65

<210> 278  
 <211> 46  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (46)  
 <223> Xaa equals stop translation

<400> 278  
 Met Pro Arg Arg Ser Arg Pro Cys Thr Leu Cys Leu Thr Leu Leu Arg  
 1 5 10 15  
 Arg Ala Leu Ser Ser His Leu Pro Ser Ala Cys Gln Ser Pro Arg Arg  
 20 25 30  
 Arg Val Gln Gly Gln Val Leu Lys Arg Leu Lys Pro Leu Xaa  
 35 40 45

<210> 279  
 <211> 40  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (40)  
 <223> Xaa equals stop translation

<400> 279  
 Met Pro Leu Thr Leu Pro Ser Arg Leu Ala Gly Gly Asn Val Phe Leu  
 1 5 10 15  
 Ile Ile Phe Thr Pro Gly Phe Cys Pro Gly Arg Val Asn Val Glu Ile  
 20 25 30  
 Pro Gln Arg Met Leu Asp Glu Xaa  
 35 40

<210> 280  
 <211> 11



<212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (11)  
 <223> Xaa equals stop translation

<400> 280  
 Met Ser Arg Arg Glu Asn Lys Phe Leu Leu Xaa  
           1                  5                  10

<210> 281  
 <211> 282  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (65)  
 <223> Xaa equals any one of the naturally occurring L-amino acids

<220>  
 <221> misc feature  
 <222> (199)  
 <223> Xaa equals any one of the naturally occurring L-amino acids

<220>  
 <221> misc feature  
 <222> (227)  
 <223> Xaa equals any one of the naturally occurring L-amino acids

<220>  
 <221> misc feature  
 <222> (276)  
 <223> Xaa equals any one of the naturally occurring L-amino acids

<220>  
 <221> misc feature  
 <222> (282)  
 <223> Xaa equals stop translation

<400> 281  
 Met Gly Phe Pro Gln Arg Gln Pro Gly Leu Ser Gly Leu Leu Leu  
           1                  5                  10                  15

Val Trp Ala Leu Ala Trp Pro Leu Pro Cys Met Ser Leu Glu Leu Ile  
                   20                  25                  30

Pro Tyr Thr Pro Gln Ile Thr Ala Trp Asp Leu Glu Gly Lys Val Thr  
           35                  40                  45

Ala Thr Thr Phe Ser Leu Glu Gln Pro Arg Cys Val Leu Asp Gly Leu  
           50                  55                  60

Xaa Gly Val Ala Ser Thr Ile Trp Leu Val Val Ala Phe Ser Asn Ala  
           65                  70                  75                  80

Ser Arg Asp Phe Gln Asn Pro Gln Thr Arg Ala Glu Ile Pro Ala Phe

146

85                      90                      95  
 Pro Arg Leu Leu Thr Glu Gly His Tyr Met Thr Leu Pro Leu Ser Leu  
                     100                      105                      110  
 Asp Gln Leu Pro Cys Gln Asp Pro Ala Gly Gly Gly Arg Asp Val Pro  
                     115                      120                      125  
 Leu Leu Arg Val Gly Asn Asp Pro Gly Cys Leu Ala Asp Leu Leu Gln  
                     130                      135                      140  
 Pro Pro Tyr Cys Asn Ser Pro Leu Pro Ser Pro Gly Pro Tyr Arg Val  
                     145                      150                      155                      160  
 Lys Phe Leu Leu Met Asp Ala Arg Gly Ser Pro Gln Ala Glu Thr Arg  
                     165                      170                      175  
 Trp Ser Asp Pro Ile Ala Leu His Gln Gly Lys Ser Pro Ala Ser Ile  
                     180                      185                      190  
 Asp Thr Trp Pro Gly Arg Xaa Ser Gly Gly Met Ile Val Ile Thr Ser  
                     195                      200                      205  
 Ile Leu Ser Ser Leu Ala Ser Leu Leu Leu Leu Ala Phe Leu Ala Ala  
                     210                      215                      220  
 Ser Thr Xaa Arg Phe Ser Ser Leu Trp Trp Pro Glu Glu Ala Pro Glu  
                     225                      230                      235                      240  
 Gln Leu Arg Ile Gly Ser Phe Met Gly Lys Arg Tyr Met Thr His His  
                     245                      250                      255  
 Ile Pro Pro Ser Glu Ala Ala Thr Leu Pro Val Gly Cys Glu Pro Gly  
                     260                      265                      270  
 Leu Asp Pro Xaa Pro Ser Leu Ser Pro Xaa  
                     275                      280

<210> 282  
 <211> 47  
 <212> PRT  
 <213> Homo sapiens

<400> 282  
 Met Leu Pro Ile His Leu Gln Trp Ala Cys Ala Phe Arg Ser Phe Leu  
                     1                      5                      10                      15  
 Leu Gly Ile Asp Ser Ser Met Phe Val Leu Phe Gln His Pro Arg Leu  
                     20                      25                      30  
 Lys Asp Thr Lys Ser Ser Arg Val Ile Glu Pro Thr Leu Thr Asn  
                     35                      40                      45

<210> 283  
 <211> 23  
 <212> PRT  
 <213> Homo sapiens

147

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (23)

&lt;223&gt; Xaa equals stop translation

&lt;400&gt; 283

Met Ile Leu Leu Ala Phe Phe Ile Leu Leu Tyr Leu Thr Ser Phe Ser  
1 5 10 15

Leu Ala Arg Ser Leu Pro Xaa  
20

&lt;210&gt; 284

&lt;211&gt; 21

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (21)

&lt;223&gt; Xaa equals stop translation

&lt;400&gt; 284

Ser Ser Ser Cys Met Pro Arg Lys Leu Asp Trp Phe Ser Lys Lys Val  
1 5 10 15

Phe Leu Phe Phe Xaa  
20

&lt;210&gt; 285

&lt;211&gt; 122

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 285

Met Gln Ala Leu Pro Pro Gly Phe Lys Gln Phe Ser Cys Leu Ser Leu  
1 5 10 15

Pro Ser Arg Trp Asp Tyr Gly Cys Ala Thr Gln His Pro Ala Asn Phe  
20 25 30

Cys Ile Phe Arg Arg Asp Arg Val Ser His Val Gly Gln Ala Gly Leu  
35 40 45

Lys Leu Leu Thr Ser Val Asp Pro Pro Ala Trp Ala Ser Gln Ser Ala  
50 55 60

Gly Ile Thr Gly Lys Ser His Cys Ala Gln Leu His Cys Cys Cys Phe  
65 70 75 80

Leu Leu Leu Val Lys Arg Asp Gln Pro Leu Glu Lys Cys Leu Arg Leu  
85 90 95

Phe Lys Gly Arg Ile Leu Cys Arg Gln Pro His Tyr Arg Leu Leu Ser  
100 105 110

Asp Glu Cys Pro Gly Leu Leu Gln Asn Pro  
115 120

148

<210> 286  
<211> 27  
<212> PRT  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (27)  
<223> Xaa equals stop translation

<400> 286  
Met Ile His Leu Ser Arg Phe Tyr Leu Leu Leu Ile Met Leu Pro His  
1 5 10 15

Val Leu Phe Phe Thr Gly Asp Leu His Ser Xaa  
20 25

<210> 287  
<211> 8  
<212> PRT  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (8)  
<223> Xaa equals stop translation

<400> 287  
Met Tyr Lys Cys Trp Tyr Arg Xaa  
1 5

<210> 288  
<211> 29  
<212> PRT  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (2)  
<223> Xaa equals any one of the naturally occurring L-amino acids

<220>  
<221> misc feature  
<222> (29)  
<223> Xaa equals stop translation

<400> 288  
Met Xaa Leu Asn Lys Thr Lys Ser Leu Thr Leu Leu Glu Leu Val Phe  
1 5 10 15

Leu Pro Gly Glu Thr Val Ser Lys Pro Ser Thr Lys Xaa  
20 25

<210> 289  
<211> 52

149

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 289

Ser Thr His Ala Ser Val Gln Lys Lys Asp Leu Thr Lys Phe Ser Ala  
1 5 10 15

His Ser Trp Leu Lys Lys Lys Lys Thr Phe Arg Lys Met Ile Met Glu  
20 25 30

Glu Ile Phe Leu Asn Leu Ile Lys Asn Ile Tyr Lys Ser Pro Tyr Ser  
35 40 45

Gln Cys Asn Thr  
50

&lt;210&gt; 290

&lt;211&gt; 17

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 290

Val Arg Ser Glu Lys Gly Phe Asp Lys Ile Gln Cys Pro Phe Met Val  
1 5 10 15

Lys

&lt;210&gt; 291

&lt;211&gt; 46

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 291

Phe Ser Lys Pro Ser Ser Tyr Lys Thr Tyr Ile Pro Lys Ile Asn Leu  
1 5 10 15

His Phe Tyr Ile Leu Leu Met Asn Ile Trp Glu Thr Ile Lys Ile Val  
20 25 30

Pro Leu Asn Asn Cys Phe Thr Lys Met Asn Tyr Leu Gly Ile  
35 40 45

&lt;210&gt; 292

&lt;211&gt; 14

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 292

Lys Lys Glu Thr Lys Leu Ser Leu Phe Ala Asn Asp Met Ile  
1 5 10

&lt;210&gt; 293

&lt;211&gt; 23

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

150

&lt;400&gt; 293

Ser Pro Leu Leu Phe Asn Ile Leu Leu Glu Val Leu Ser Ser Ala Val  
 1 5 10 15

Arg Lys Glu Lys Glu Leu Lys  
 20

&lt;210&gt; 294

&lt;211&gt; 122

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 294

Leu Arg Arg Pro Ser Thr Pro Leu Arg Arg Pro Trp Leu His Leu Gln  
 1 5 10 15

Leu Pro Arg Ile Ser Leu Gly Asp Gln Arg Leu Ala Gln Ser Ala Glu  
 20 25 30

Met Tyr His Tyr Gln His Gln Arg Gln Gln Met Leu Ser Leu Glu Arg  
 35 40 45

His Lys Glu Pro Pro Lys Glu Leu Asp Thr Ala Leu Arg Met Arg Arg  
 50 55 60

Met Arg Thr Glu Thr Ser Arg Cys Thr Ser Ala Arg Ala Trp Pro Arg  
 65 70 75 80

Pro Gly Lys Trp Arg Cys Ala Thr Ile Cys Ser Thr Thr Pro His Cys  
 85 90 95

Pro Arg Pro Cys Arg Pro Pro Ala His Arg Leu His Cys His Asp Leu  
 100 105 110

Glu Ala Asp Arg Arg Pro Leu Ala Pro Arg  
 115 120

&lt;210&gt; 295

&lt;211&gt; 60

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 295

Arg Ala Thr Gln Gly Ala Gly His Gly Ser Ser Asp Glu Glu Asn Glu  
 1 5 10 15

Asp Gly Asp Phe Thr Val Tyr Glu Cys Pro Gly Met Ala Pro Thr Gly  
 20 25 30

Glu Met Glu Val Arg Asn His Leu Phe Asp His Ala Ala Leu Ser Ala  
 35 40 45

Pro Leu Pro Ala Pro Ser Ser Pro Leu Ala Leu Pro  
 50 55 60

&lt;210&gt; 296

<211> 47  
<212> PRT  
<213> Homo sapiens

<400> 296  
Lys Ala Glu Tyr Ala Thr Ala Lys Ala Leu Ala Thr Pro Ala Ala Thr  
1 5 10 15  
Pro Asp Leu Ala Trp Gly Pro Ala Pro Gly Thr Glu Arg Gly Asp Val  
20 25 30  
Pro Leu Pro Ala Pro Thr Ala Thr Asp Val Val Pro Gly Ala Ala  
35 40 45

<210> 297  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 297  
Ser Ala Glu Met Tyr His Tyr Gln His Gln Arg Gln Gln Met Leu  
1 5 10 15

<210> 298  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 298  
Leu Glu Arg His Lys Glu Pro Pro Lys Glu Leu  
1 5 10

<210> 299  
<211> 12  
<212> PRT  
<213> Homo sapiens

<400> 299  
Ala Lys Cys Pro Pro Gly Ala His Ala Cys Gly Pro  
1 5 10

<210> 300  
<211> 9  
<212> PRT  
<213> Homo sapiens

<400> 300  
Pro Val His Met Ser Pro Leu Glu Pro  
1 5

<210> 301  
<211> 12  
<212> PRT  
<213> Homo sapiens

&lt;400&gt; 301

Trp Cys Arg Leu Gln Arg Glu Ile Arg Leu Thr Gln  
1 5 10

&lt;210&gt; 302

&lt;211&gt; 18

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 302

Ser Ser Asp Glu Glu Asn Glu Asp Gly Asp Phe Thr Val Tyr Glu Cys  
1 5 10 15

Pro Gly

&lt;210&gt; 303

&lt;211&gt; 10

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 303

Ala Pro Thr Gly Glu Met Glu Val Arg Asn  
1 5 10

&lt;210&gt; 304

&lt;211&gt; 10

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 304

Cys Pro Gly Ser Leu Asp Cys Ala Leu Lys  
1 5 10

&lt;210&gt; 305

&lt;211&gt; 8

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 305

Arg Ser Cys Lys Glu Ile Lys Asp  
1 5

&lt;210&gt; 306

&lt;211&gt; 13

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 306

Gly Gly Gly Trp Thr Leu Val Ala Ser Val His Glu Asn  
1 5 10

&lt;210&gt; 307

&lt;211&gt; 19



<212> PRT

<213> Homo sapiens

<400> 307

Ala Asp Tyr Pro Glu Gly Asp Gly Asn Trp Ala Asn Tyr Asn Thr Phe  
1 5 10 15

Gly Ser Ala

<210> 308

<211> 14

<212> PRT

<213> Homo sapiens

<400> 308

Ala Thr Ser Asp Asp Tyr Lys Asn Pro Gly Tyr Tyr Asp Ile  
1 5 10

<210> 309

<211> 11

<212> PRT

<213> Homo sapiens

<400> 309

Cys Ile Gly Gly Gly Gly Tyr Phe Pro Glu Ala  
1 5 10

<210> 310

<211> 11

<212> PRT

<213> Homo sapiens

<400> 310

Glu Ile Thr Glu Ala Ala Val Leu Leu Phe Tyr  
1 5 10

<210> 311

<211> 300

<212> PRT

<213> Homo sapiens

<220>

<221> misc feature

<222> (4)

<223> Xaa equals any one of the naturally occurring L-amino acids

<220>

<221> misc feature

<222> (62)

<223> Xaa equals any one of the naturally occurring L-amino acids

<400> 311

Lys His Glu Xaa His Gln Val Ser Asp Gly Ala Leu Arg Cys Phe Ala  
1 5 10 15

154

Ser Leu Ala Asp Arg Phe Thr Arg Arg Gly Val Asp Pro Ala Pro Leu  
 20 25 30  
 Ala Lys His Gly Leu Thr Glu Glu Leu Leu Ser Arg Met Ala Ala Ala  
 35 40 45  
 Gly Gly Thr Val Ser Gly Pro Ser Ser Ala Cys Lys Pro Xaa Arg Ser  
 50 55 60  
 Thr Thr Gly Ala Pro Ser Thr Thr Ala Asp Ser Lys Leu Ser Asn Gln  
 65 70 75 80  
 Val Ser Thr Ile Val Ser Leu Leu Ser Thr Leu Cys Arg Gly Ser Pro  
 85 90 95  
 Val Val Thr His Asp Leu Leu Arg Ser Glu Leu Pro Asp Ser Ile Glu  
 100 105 110  
 Ser Ala Leu Gln Gly Asp Glu Arg Cys Val Leu Asp Thr Met Arg Leu  
 115 120 125  
 Val Asp Phe Leu Leu Val Leu Leu Phe Glu Gly Arg Lys Ala Leu Pro  
 130 135 140  
 Lys Ser Ser Ala Gly Ser Thr Gly Arg Ile Pro Gly Leu Arg Arg Leu  
 145 150 155 160  
 Asp Ser Ser Gly Glu Arg Ser His Arg Gln Leu Ile Asp Cys Ile Arg  
 165 170 175  
 Ser Lys Asp Thr Asp Ala Leu Ile Asp Ala Ile Asp Thr Gly Ala Phe  
 180 185 190  
 Glu Val Asn Phe Met Asp Asp Val Gly Gln Thr Leu Leu Asn Trp Ala  
 195 200 205  
 Ser Ala Phe Gly Thr Gln Glu Met Val Glu Phe Leu Cys Glu Arg Gly  
 210 215 220  
 Ala Asp Val Asn Arg Gly Gln Arg Ser Ser Ser Leu His Tyr Ala Ala  
 225 230 235 240  
 Cys Phe Gly Arg Pro Gln Val Ala Lys Thr Leu Leu Arg His Gly Ala  
 245 250 255  
 Asn Pro Asp Leu Arg Asp Glu Asp Gly Lys Thr Pro Leu Asp Lys Ala  
 260 265 270  
 Arg Glu Arg Gly His Ser Glu Val Val Ala Ile Leu Gln Ser Pro Gly  
 275 280 285  
 Asp Trp Met Cys Pro Val Asn Lys Gly Asp Asp Lys  
 290 295 300

&lt;210&gt; 312

&lt;211&gt; 17

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

155

&lt;400&gt; 312

Pro Leu Asp Lys Ala Arg Glu Arg Gly His Ser Glu Val Val Ala Ile  
1 5 10 15

Leu

&lt;210&gt; 313

&lt;211&gt; 15

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 313

Ala Lys Thr Leu Leu Arg His Gly Ala Asn Pro Asp Leu Arg Asp  
1 5 10 15

&lt;210&gt; 314

&lt;211&gt; 52

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (26)

&lt;223&gt; Xaa equals any one of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (29)

&lt;223&gt; Xaa equals any one of the naturally occurring L-amino acids

&lt;400&gt; 314

Asp Cys Asn Arg Asp Tyr His Lys Ala Phe Gly Asn Leu Arg Ser Pro  
1 5 10 15

Gly Trp Pro Asp Asn Tyr Asp Asn Asp Xaa Asp Cys Xaa Val Thr Leu  
20 25 30

Thr Ala Pro Gln Asn His His Ser Gly Ile Val Glu Asn Ala Glu Thr  
35 40 45

Ile Ser Trp Arg  
50

&lt;210&gt; 315

&lt;211&gt; 15

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 315

Phe Gly Asn Leu Arg Ser Pro Gly Trp Pro Asp Asn Tyr Asp Asn  
1 5 10 15

&lt;210&gt; 316

&lt;211&gt; 16

&lt;212&gt; PRT

<213> Homo sapiens

<220>

<221> misc feature

<222> (6)

<223> Xaa equals any one of the naturally occurring L-amino acids

<400> 316

Ala	Pro	Gln	Asn	His	Xaa	Leu	Lys	Cys	Arg	Asn	Asp	Phe	Leu	Glu	Val
1				5					10					15	

<210> 317

<211> 20

<212> PRT

<213> Homo sapiens

<400> 317

Ala	Ser	Ile	Asp	Thr	Trp	Pro	Gly	Arg	Arg	Ser	Gly	Gly	Met	Ile	Val
1				5					10					15	

Ile	Thr	Ser	Ile
			20

<210> 318

<211> 41

<212> PRT

<213> Homo sapiens

<400> 318

Gly	Ser	Pro	Gln	Ala	Glu	Thr	Arg	Trp	Ser	Asp	Pro	Ile	Ala	Leu	His
1				5					10					15	

Gln	Gly	Lys	Ser	Pro	Ala	Ser	Ile	Asp	Thr	Trp	Pro	Gly	Arg	Arg	Ser
			20					25					30		

Gly	Gly	Met	Ile	Val	Ile	Thr	Ser	Ile
		35					40	

<210> 319

<211> 43

<212> PRT

<213> Homo sapiens

<220>

<221> misc feature

<222> (2)

<223> Xaa equals any one of the naturally occurring L-amino acids

<400> 319

Val	Xaa	Asp	Ile	Thr	Phe	Asp	Pro	Asp	Thr	Ala	His	Lys	Tyr	Leu	Arg
1				5					10					15	

Leu	Gln	Glu	Glu	Asn	Arg	Lys	Val	Thr	Asn	Thr	Thr	Pro	Trp	Glu	His
			20					25					30		

Pro Tyr Pro Asp Leu Pro Ser Arg Phe Leu His  
           35                          40

<210> 320  
 <211> 19  
 <212> PRT  
 <213> Homo sapiens

<400> 320  
 Leu Tyr Leu His Arg Tyr Tyr Phe Glu Val Glu Ile Phe Gly Ala Gly  
       1                  5                  10                  15

Thr Tyr Val

<210> 321  
 <211> 22  
 <212> PRT  
 <213> Homo sapiens

<400> 321  
 Ser Cys Ile Ser Gly Asn Asn Phe Ser Trp Ser Leu Gln Trp Asn Gly  
       1                  5                  10                  15

Lys Glu Phe Thr Ala Trp  
                   20

<210> 322  
 <211> 17  
 <212> PRT  
 <213> Homo sapiens

<400> 322  
 Thr Pro Leu Lys Ala Gly Pro Phe Trp Ser Ser Gly Ser Ile Leu Thr  
       1                  5                  10                  15

Ser

<210> 323  
 <211> 39  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (32)  
 <223> Xaa equals any one of the naturally occurring L-amino acids

<400> 323  
 Ser Val Ser Glu Val Lys Ala Val Ala Glu Met Gln Phe Gly Glu Leu  
       1                  5                  10                  15

Leu Ala Ala Val Arg Lys Ala Gln Ala Asn Val Met Leu Phe Leu Xaa  
                   20                  25                  30

Glu Lys Glu Gln Ala Ala Leu  
35

<210> 324

<211> 43

<212> PRT

<213> Homo sapiens

<400> 324

Glu Lys Ser Lys Gln Glu Leu Glu Thr Met Ala Ala Ile Ser Asn Thr  
1 5 10 15

Val Gln Phe Leu Glu Glu Tyr Cys Lys Phe Lys Asn Thr Glu Asp Ile  
20 25 30

Thr Phe Pro Ser Val Tyr Ile Gly Leu Lys Asp  
35 40

<210> 325

<211> 29

<212> PRT

<213> Homo sapiens

<220>

<221> misc feature

<222> (26)

<223> Xaa equals any one of the naturally occurring L-amino acids

<400> 325

Leu Glu Asn Tyr Lys Lys Lys Leu Gln Glu Phe Ser Lys Glu Glu Glu  
1 5 10 15

Tyr Asp Ile Arg Thr Gln Val Ser Ala Xaa Val Gln Arg  
20 25

<210> 326

<211> 38

<212> PRT

<213> Homo sapiens

<400> 326

Gly Val Tyr Ile Asp Phe Pro Gly Gly Ile Leu Ser Phe Tyr Gly Val  
1 5 10 15

Glu Tyr Asp Ser Met Thr Leu Val His Lys Phe Ala Cys Lys Phe Ser  
20 25 30

Glu Pro Val Tyr Ala Ala  
35

<210> 327

<211> 196

<212> PRT

<213> Homo sapiens

159

&lt;400&gt; 327

Ser Lys Ile Lys Tyr Asp Trp Tyr Gln Thr Glu Ser Gln Val Val Ile  
 1 5 10 15

Thr Leu Met Ile Lys Asn Val Gln Lys Asn Asp Val Asn Val Glu Phe  
 20 25 30

Ser Glu Lys Glu Leu Ser Ala Leu Val Lys Leu Pro Ser Gly Glu Asp  
 35 40 45

Tyr Asn Leu Lys Leu Glu Leu Leu His Pro Ile Ile Pro Glu Gln Ser  
 50 55 60

Thr Phe Lys Val Leu Ser Thr Lys Ile Glu Ile Lys Leu Lys Lys Pro  
 65 70 75 80

Glu Ala Val Arg Trp Glu Lys Leu Glu Gly Gln Gly Asp Val Pro Thr  
 85 90 95

Pro Lys Gln Phe Val Ala Asp Val Lys Asn Leu Tyr Pro Ser Ser Ser  
 100 105 110

Pro Tyr Thr Arg Asn Trp Asp Lys Leu Val Gly Glu Ile Lys Glu Glu  
 115 120 125

Glu Lys Asn Glu Lys Leu Glu Gly Asp Ala Ala Leu Asn Arg Leu Phe  
 130 135 140

Gln Gln Ile Tyr Ser Asp Gly Ser Asp Glu Val Lys Arg Ala Met Asn  
 145 150 155 160

Lys Ser Phe Met Glu Ser Gly Gly Thr Val Leu Ser Thr Asn Trp Ser  
 165 170 175

Asp Val Gly Lys Arg Lys Val Glu Ile Asn Pro Pro Asp Asp Met Glu  
 180 185 190

Trp Lys Lys Tyr  
 195

&lt;210&gt; 328

&lt;211&gt; 39

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 328

Gly Asp Ala Ala Leu Asn Arg Leu Phe Gln Gln Ile Tyr Ser Asp Gly  
 1 5 10 15

Ser Asp Glu Val Lys Arg Ala Met Asn Lys Ser Phe Met Glu Ser Gly  
 20 25 30

Gly Thr Val Leu Ser Thr Asn  
 35

&lt;210&gt; 329

&lt;211&gt; 23

&lt;212&gt; PRT

160

&lt;213&gt; Homo sapiens

&lt;400&gt; 329

Asp Trp Tyr Gln Thr Glu Ser Gln Val Val Ile Thr Leu Met Ile Lys  
 1 5 10 15

Asn Val Gln Lys Asn Asp Val  
 20

&lt;210&gt; 330

&lt;211&gt; 162

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1)

&lt;223&gt; Xaa equals any one of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (33)

&lt;223&gt; Xaa equals any one of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (48)

&lt;223&gt; Xaa equals any one of the naturally occurring L-amino acids

&lt;400&gt; 330

Xaa Leu Trp Asp Pro Gly Leu Pro Gly Val Cys Arg Cys Gly Ser Ile  
 1 5 10 15

Val Leu Lys Ser Ala Phe Ser Val Gly Ile Thr Thr Ser Tyr Pro Glu  
 20 25 30

Xaa Arg Leu Pro Ile Ile Phe Asn Lys Val Leu Leu Pro Arg Gly Xaa  
 35 40 45

Ala Leu Gln Pro Cys His Arg Gly Ser Ser Ser Val Leu Ser Gln Gly  
 50 55 60

Ile Tyr Tyr Phe Ser Tyr Asp Ile Thr Leu Ala Asn Lys His Leu Ala  
 65 70 75 80

Ile Gly Leu Val His Asn Gly Gln Tyr Arg Ile Lys Thr Phe Asp Ala  
 85 90 95

Asn Thr Gly Asn His Asp Val Ala Ser Gly Ser Thr Val Ile Tyr Leu  
 100 105 110

Gln Pro Glu Asp Glu Val Trp Leu Glu Ile Phe Phe Thr Asp Gln Asn  
 115 120 125

Gly Leu Phe Ser Asp Pro Gly Trp Ala Asp Ser Leu Phe Ser Gly Phe  
 130 135 140

Leu Leu Tyr Val Asp Thr Asp Tyr Leu Asp Ser Ile Ser Glu Asp Asp  
 145 150 155 160



Glu Leu

<210> 331

<211> 15

<212> PRT

<213> Homo sapiens

<400> 331

Gly Ser Ile Val Leu Lys Ser Ala Phe Ser Val Gly Ile Thr Thr  
1 5 10 15

<210> 332

<211> 14

<212> PRT

<213> Homo sapiens

<400> 332

Gly Ile Tyr Tyr Phe Ser Tyr Asp Ile Thr Leu Ala Asn Lys  
1 5 10

<210> 333

<211> 13

<212> PRT

<213> Homo sapiens

<400> 333

Asp Ser Leu Phe Ser Gly Phe Leu Leu Tyr Val Asp Thr  
1 5 10

<210> 334

<211> 13

<212> PRT

<213> Homo sapiens

<400> 334

Asn His Asp Val Ala Ser Gly Ser Thr Val Ile Tyr Leu  
1 5 10

<210> 335

<211> 89

<212> PRT

<213> Homo sapiens

<220>

<221> misc feature

<222> (60)

<223> Xaa equals any one of the naturally occurring L-amino acids

<220>

<221> misc feature

<222> (75)

<223> Xaa equals any one of the naturally occurring L-amino acids

162

&lt;400&gt; 335

Glu Asn Phe Leu Leu Arg Tyr Lys Gly Pro Ser Asp His Trp Ile Gly  
 1 5 10 15  
 Leu Ser Arg Glu Gln Gly Gln Pro Trp Lys Trp Ile Asn Gly Thr Glu  
 20 25 30  
 Trp Thr Arg Gln Leu Val Met Lys Glu Asp Gly Ala Asn Leu Tyr Val  
 35 40 45  
 Ala Lys Val Ser Gln Val Pro Arg Met Asn Pro Xaa Leu Ser Trp Val  
 50 55 60  
 Leu Leu Cys Tyr Pro Gly Trp Ser Ala Val Xaa Thr Ile Val Ala His  
 65 70 75 80  
 Cys Ser Leu Asp Phe Pro Gly Ser Lys  
 85

&lt;210&gt; 336

&lt;211&gt; 63

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 336

Glu Leu Thr Ala Ile Lys Ser His Gln Tyr Val Leu Gln Ala Ala Cys  
 1 5 10 15  
 Pro Glu Ser Trp Ile Gly Phe Gln Arg Lys Cys Phe Tyr Phe Ser Asp  
 20 25 30  
 Asp Thr Lys Asn Trp Thr Ser Ser Gln Arg Phe Cys Asp Ser Gln Asp  
 35 40 45  
 Ala Asp Leu Ala Gln Val Glu Ser Phe Gln Glu Leu Val Arg Lys  
 50 55 60

&lt;210&gt; 337

&lt;211&gt; 17

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 337

Trp Ile Gly Leu Ser Arg Glu Gln Gly Gln Pro Trp Lys Trp Ile Asn  
 1 5 10 15  
 Gly

&lt;210&gt; 338

&lt;211&gt; 12

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 338

Cys Pro Glu Ser Trp Ile Gly Phe Gln Arg Lys Cys  
 1 5 10

<210> 339  
<211> 16  
<212> PRT  
<213> Homo sapiens

<400> 339  
Asn Phe Leu Leu Arg Tyr Lys Gly Pro Ser Asp His Trp Ile Gly Leu  
1 5 10 15

<210> 340  
<211> 50  
<212> PRT  
<213> Homo sapiens

<400> 340  
Ala Ser His Leu Arg Leu Leu Ser Ser Trp Asp Tyr Arg Phe Pro Ile  
1 5 10 15  
Leu Gly Ala Gly Glu Cys Ala Tyr Leu Asn Asp Lys Gly Ala Ser Ser  
20 25 30  
Ala Arg His Tyr Thr Glu Arg Lys Trp Ile Cys Ser Lys Ser Asp Ile  
35 40 45  
His Val  
50

<210> 341  
<211> 89  
<212> PRT  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (60)  
<223> Xaa equals any one of the naturally occurring L-amino acids

<220>  
<221> misc feature  
<222> (75)  
<223> Xaa equals any one of the naturally occurring L-amino acids

<400> 341  
Glu Asn Phe Leu Leu Arg Tyr Lys Gly Pro Ser Asp His Trp Ile Gly  
1 5 10 15  
Leu Ser Arg Glu Gln Gly Gln Pro Trp Lys Trp Ile Asn Gly Thr Glu  
20 25 30  
Trp Thr Arg Gln Leu Val Met Lys Glu Asp Gly Ala Asn Leu Tyr Val  
35 40 45  
Ala Lys Val Ser Gln Val Pro Arg Met Asn Pro Xaa Leu Ser Trp Val

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<210> 343
<211> 109
<212> PRT
<213> Homo sapiens

<220>
<221> misc feature
<222> (24)
<223> Xaa equals any one of the naturally occurring L-amino acids

<220>
<221> misc feature
<222> (25)
<223> Xaa equals any one of the naturally occurring L-amino acids
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&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (31)

&lt;223&gt; Xaa equals any one of the naturally occurring L-amino acids

&lt;400&gt; 343

Leu Lys Gly Arg Glu Ala Gly Ala Gly Pro Gly Thr Ala Gly Ala Pro  
 1 5 10 15

Gly Arg Glu Asp Ala Asn Gly Xaa Xaa Arg Gly Arg Gly Gly Xaa His  
 20 25 30

Gln Leu Tyr Leu Trp Val Asp Asn Ile Pro Leu Ser Arg Pro Lys Arg  
 35 40 45

Asn Leu Ser Arg Asp Phe Ser Asp Gly Val Leu Val Ala Glu Val Ile  
 50 55 60

Lys Phe Tyr Phe Pro Lys Met Val Glu Met His Asn Tyr Val Gly Thr  
 65 70 75 80

Ser Ser Leu Gln Gln Lys Leu Ser Asn Trp Gly His Leu Asn Arg Lys  
 85 90 95

Val Leu Lys Arg Leu Asn Phe Ser Val Pro Asp Asp Val  
 100 105

&lt;210&gt; 344

&lt;211&gt; 187

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 344

Ala Lys Asn Ser Gln Lys Glu Glu Asn Pro Glu His Val Glu Ile Gln  
 1 5 10 15

Lys Met Met Asp Ser Leu Phe Leu Lys Leu Asp Ala Leu Ser Asn Phe  
 20 25 30

His Phe Ile Pro Lys Pro Pro Val Pro Glu Ile Lys Val Val Ser Asn  
 35 40 45

Leu Pro Ala Ile Thr Met Glu Glu Val Ala Pro Val Ser Val Ser Asp  
 50 55 60

Ala Ala Leu Leu Ala Pro Glu Glu Ile Lys Glu Lys Asn Lys Ala Gly  
 65 70 75 80

Asp Ile Lys Thr Ala Ala Glu Lys Thr Ala Thr Asp Lys Lys Arg Glu  
 85 90 95

Arg Arg Lys Lys Lys Tyr Gln Lys Arg Met Lys Ile Lys Glu Lys Glu  
 100 105 110

Lys Arg Arg Lys Leu Leu Glu Lys Ser Ser Val Asp Gln Ala Gly Lys  
 115 120 125

Tyr Ser Lys Thr Val Ala Ser Glu Lys Leu Lys Gln Leu Thr Lys Thr

166

130 135 140

Gly Lys Ala Ser Phe Ile Lys Val Arg Thr Arg Glu Arg Lys Leu Leu  
 145 150 155 160

Lys Gly Thr Phe Val Gly Glu Val Asp Ser Lys Cys Trp Val Thr Gly  
 165 170 175

Met Ser Glu Pro Ala Asp Ser Pro Pro Val Gly  
 180 185

<210> 345  
 <211> 51  
 <212> PRT  
 <213> Homo sapiens

<400> 345

Leu Gln Asp Glu Gly Lys Asp Lys Ala Leu Lys Ser Ser Gln Ala Phe  
 1 5 10 15

Phe Ser Lys Leu Gln Asp Gln Val Lys Met Gln Ile Asn Asp Ala Lys  
 20 25 30

Lys Thr Glu Lys Lys Lys Lys Lys Arg Gln Asp Ile Ser Val His Lys  
 35 40 45

Leu Lys Leu  
 50

<210> 346  
 <211> 29  
 <212> PRT  
 <213> Homo sapiens

<400> 346

Asp Glu Gly Lys Asp Lys Ala Leu Lys Ser Ser Gln Ala Phe Phe Ser  
 1 5 10 15

Lys Leu Gln Asp Gln Val Lys Met Gln Ile Asn Asp Ala  
 20 25

<210> 347  
 <211> 28  
 <212> PRT  
 <213> Homo sapiens

<400> 347

Glu Glu Asn Pro Glu His Val Glu Ile Gln Lys Met Met Asp Ser Leu  
 1 5 10 15

Phe Leu Lys Leu Asp Ala Leu Ser Asn Phe His Phe  
 20 25

<210> 348  
 <211> 13  
 <212> PRT

<213> Homo sapiens

<400> 348

Ser Asn Leu Pro Ala Ile Thr Met Glu Glu Val Ala Pro  
1 5 10

<210> 349

<211> 31

<212> PRT

<213> Homo sapiens

<400> 349

Ser Ser Val Asp Gln Ala Gly Lys Tyr Ser Lys Thr Val Ala Ser Glu  
1 5 10 15

Lys Leu Lys Gln Leu Thr Lys Thr Gly Lys Ala Ser Phe Ile Lys  
20 25 30

<210> 350

<211> 23

<212> PRT

<213> Homo sapiens

<400> 350

Val Ser Val Ser Asp Ala Ala Leu Leu Ala Pro Glu Glu Ile Lys Glu  
1 5 10 15

Lys Asn Lys Ala Gly Asp Ile  
20

<210> 351

<211> 20

<212> PRT

<213> Homo sapiens

<400> 351

Met Ala Ile Pro Ala Phe Ser Ser Cys Gln Gln Ile Ser Ser Ala Ala  
1 5 10 15

Ala Leu Gln Ile  
20

<210> 352

<211> 14

<212> PRT

<213> Homo sapiens

<400> 352

Cys Asn Gly Pro Phe Lys His Phe Ser Phe Thr Val Ser Thr  
1 5 10

<210> 353

<211> 11

<212> PRT

<213> Homo sapiens

&lt;400&gt; 353

Cys Arg Trp Arg Pro Glu Ser Ala Ala Pro Cys  
1 5 10

&lt;210&gt; 354

&lt;211&gt; 12

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 354

Thr Arg Pro Gly Arg Gly Ala Gln Ala Pro Val Lys  
1 5 10

&lt;210&gt; 355

&lt;211&gt; 21

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 355

Met Val Ser Trp Met Ile Ser Arg Ala Val Val Leu Val Phe Gly Met  
1 5 10 15

Leu Tyr Pro Ala Tyr  
20

&lt;210&gt; 356

&lt;211&gt; 17

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 356

Gly Met Leu Tyr Pro Ala Tyr Tyr Ser Tyr Lys Ala Val Lys Thr Lys  
1 5 10 15

Asn

&lt;210&gt; 357

&lt;211&gt; 17

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 357

Glu Tyr Val Arg Trp Met Met Tyr Trp Ile Val Phe Ala Leu Tyr Thr  
1 5 10 15

Val

&lt;210&gt; 358

&lt;211&gt; 17

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens



&lt;400&gt; 358

Tyr Pro Ala Tyr Tyr Ser Tyr Lys Ala Val Lys Thr Lys Asn Val Lys  
 1 5 10 15

Glu

&lt;210&gt; 359

&lt;211&gt; 13

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 359

Val Ala Trp Phe Pro Leu Tyr Tyr Glu Leu Lys Ile Ala  
 1 5 10

&lt;210&gt; 360

&lt;211&gt; 186

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (181)

&lt;223&gt; Xaa equals any one of the naturally occurring L-amino acids

&lt;400&gt; 360

Met Val Ser Trp Met Ile Ser Arg Ala Val Val Leu Val Phe Gly Met  
 1 5 10 15

Leu Tyr Pro Ala Tyr Tyr Ser Tyr Lys Ala Val Lys Thr Lys Asn Val  
 20 25 30

Lys Glu Tyr Val Arg Trp Met Met Tyr Trp Ile Val Phe Ala Leu Tyr  
 35 40 45

Thr Val Ile Glu Thr Val Ala Asp Gln Thr Val Ala Trp Phe Pro Leu  
 50 55 60

Tyr Tyr Glu Leu Lys Ile Ala Phe Val Ile Trp Leu Leu Ser Pro Tyr  
 65 70 75 80

Thr Lys Gly Ala Ser Leu Ile Tyr Arg Lys Phe Leu His Pro Leu Leu  
 85 90 95

Ser Ser Lys Glu Arg Glu Ile Asp Asp Tyr Ile Val Gln Ala Lys Glu  
 100 105 110

Arg Gly Tyr Glu Thr Met Val Asn Phe Gly Arg Gln Gly Leu Asn Leu  
 115 120 125

Ala Ala Thr Ala Ala Val Thr Ala Ala Val Lys Ser Gln Gly Ala Ile  
 130 135 140

Thr Glu Arg Leu Arg Ser Phe Ser Met His Asp Leu Thr Thr Ile Gln  
 145 150 155 160

Gly Asp Glu Pro Val Gly Gln Arg Pro Tyr Gln Pro Leu Pro Glu Ala

170

165 170 175  
Lys Lys Lys Ser Xaa Gln Pro Pro Val Asn  
180 185

<210> 361  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 361  
Gln Pro Tyr Gln Val Leu Pro Ser Arg Gln Val Phe Ala Leu Ile  
1 5 10 15

<210> 362  
<211> 24  
<212> PRT  
<213> Homo sapiens

<400> 362  
Val Phe Ser Cys Ile Tyr Gly Glu Gly Tyr Ser Asn Ala His Glu Ser  
1 5 10 15

Lys Gln Met Tyr Cys Val Phe Asn  
20

<210> 363  
<211> 18  
<212> PRT  
<213> Homo sapiens

<400> 363  
Arg Asn Glu Asp Ala Cys Arg Tyr Gly Ser Ala Ile Gly Val Leu Ala  
1 5 10 15

Phe Leu

<210> 364  
<211> 17  
<212> PRT  
<213> Homo sapiens

<400> 364  
Leu Val Val Asp Ala Tyr Phe Pro Gln Ile Ser Asn Ala Thr Asp Arg  
1 5 10 15

Lys

<210> 365  
<211> 25  
<212> PRT  
<213> Homo sapiens

&lt;400&gt; 365

Ser Ala Leu Trp Thr Phe Leu Trp Phe Val Gly Phe Cys Phe Leu Thr  
1 5 10 15

Asn Gln Trp Ala Val Thr Asn Pro Lys  
20 25

&lt;210&gt; 366

&lt;211&gt; 13

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 366

Ser Leu Gln Tyr Arg Ile Arg Ile Pro Gly Arg Pro Thr  
1 5 10

&lt;210&gt; 367

&lt;211&gt; 22

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 367

Asp Leu Val Thr Tyr Thr Ser Ser Leu Gln Tyr Arg Ile Arg Ile Pro  
1 5 10 15

Gly Arg Pro Thr Arg Pro  
20

&lt;210&gt; 368

&lt;211&gt; 36

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 368

Leu Gly Asn Lys Lys Tyr Ile Asn Ile Arg Cys Leu Glu Met Gln Val  
1 5 10 15

Thr Leu Lys Ile Leu Cys Glu Ile Glu Lys Lys Glu Arg Arg Gly Thr  
20 25 30

His Cys Leu Val  
35

&lt;210&gt; 369

&lt;211&gt; 22

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 369

Val Lys Thr Ala Glu Cys Tyr Ser Ile Pro Leu Gly Ser Cys Pro Val  
1 5 10 15

Asn Ile Gln Arg Val Arg  
20

172

<210> 370  
<211> 12  
<212> PRT  
<213> Homo sapiens

<400> 370  
Ile Thr Leu Cys Leu Val Cys Ile Val Ala Asn Ala  
1 5 10

<210> 371  
<211> 24  
<212> PRT  
<213> Homo sapiens

<400> 371  
Val Thr Ala Tyr Gln Asn Gln Gln Ile Thr Arg Leu Lys Ile Asp Arg  
1 5 10 15

Asn Pro Phe Ala Lys Gly Phe Arg  
20

<210> 372  
<211> 16  
<212> PRT  
<213> Homo sapiens

<400> 372  
Gly Thr Ala Thr Val Thr Ala Tyr Gln Asn Gln Gln Ile Thr Arg Leu  
1 5 10 15

<210> 373  
<211> 24  
<212> PRT  
<213> Homo sapiens

<400> 373  
Lys Ile Asp Arg Asn Pro Phe Ala Lys Gly Phe Arg Asp Ser Gly Arg  
1 5 10 15

Asn Arg Met Gly Leu Glu Ala Leu  
20

<210> 374  
<211> 21  
<212> PRT  
<213> Homo sapiens

<400> 374  
Ser Thr Leu Leu Gln Val Leu Gly Met Ala Phe Leu Pro Leu Thr Leu  
1 5 10 15

Thr Phe Cys Leu Ala  
20

<210> 375  
<211> 30  
<212> PRT  
<213> Homo sapiens

<400> 375  
Val Glu Ser Tyr Ala Phe Trp Arg Pro Ser Leu Arg Thr Leu Thr Phe  
1 5 10 15  
Glu Asp Ile Pro Gly Ile Pro Lys Gln Gly Asn Ala Ser Ser  
20 25 30

<210> 376  
<211> 14  
<212> PRT  
<213> Homo sapiens

<400> 376  
Gln Ala Gln Ser Asp Cys Ser Cys Ser Thr Val Ser Pro Gly  
1 5 10

<210> 377  
<211> 24  
<212> PRT  
<213> Homo sapiens

<400> 377  
Val Leu Ala Gly Ile Val Met Gly Asp Leu Val Leu Thr Val Leu Ile  
1 5 10 15  
Ala Leu Ala Val Tyr Phe Leu Gly  
20

<210> 378  
<211> 37  
<212> PRT  
<213> Homo sapiens

<400> 378  
Val Pro Arg Gly Arg Gly Ala Ala Glu Ala Thr Arg Lys Gln Arg Ile  
1 5 10 15  
Thr Glu Thr Glu Ser Pro Tyr Gln Glu Leu Gln Gly Gln Arg Ser Asp  
20 25 30

Val Tyr Ser Asp Leu  
35

<210> 379  
<211> 22  
<212> PRT  
<213> Homo sapiens

<400> 379

174

Glu Thr Glu Ser Pro Tyr Gln Glu Leu Gln Gly Gln Arg Ser Asp Val  
1 5 10 15

Tyr Ser Asp Leu Asn Thr  
20

&lt;210&gt; 380

&lt;211&gt; 28

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 380

Phe Leu Cys Ala Leu Ser Pro Leu Gly Gln Leu Leu Gln Asp Arg Tyr  
1 5 10 15

Gly Trp Arg Gly Gly Phe Leu Ile Leu Gly Gly Leu  
20 25

&lt;210&gt; 381

&lt;211&gt; 27

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (22)

&lt;223&gt; Xaa equals any one of the naturally occurring L-amino acids

&lt;400&gt; 381

Leu Leu Asn Cys Cys Val Cys Ala Ala Leu Met Arg Pro Leu Val Val  
1 5 10 15

Thr Ala Gln Pro Gly Xaa Gly Pro Pro Arg Pro  
20 25

&lt;210&gt; 382

&lt;211&gt; 25

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (5)

&lt;223&gt; Xaa equals any one of the naturally occurring L-amino acids

&lt;400&gt; 382

Ser Arg Arg Leu Xaa Asp Leu Ser Val Phe Arg Asp Arg Gly Phe Val  
1 5 10 15

Leu Tyr Ala Val Ala Ala Ser Val Met  
20 25

&lt;210&gt; 383

&lt;211&gt; 57

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

175

&lt;400&gt; 383

Met Met Ala Thr Pro Ser Thr Arg Pro Pro Pro Pro Ala Ala Ser Thr  
 1 5 10 15

Thr Ser Ala Thr Ala Pro Ala Leu Pro Pro Arg Pro Pro Trp Pro Trp  
 20 25 30

Pro Pro Ser Ser Trp Pro Pro Ser Gly Val Ser Ser Lys Ala Pro Glu  
 35 40 45

Ala Asp Pro Leu Lys Asn Lys Ala Leu  
 50 55

&lt;210&gt; 384

&lt;211&gt; 76

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 384

Leu Leu Leu Thr Ser Pro Leu Pro Arg Cys Pro Pro Ala Cys Ser His  
 1 5 10 15

Asp Ala Pro Ala His Pro Asp Pro Gly Gly Pro His Gly Leu Thr Ser  
 20 25 30

Gly Pro Gly Leu Gly Leu Pro Arg Val Cys Leu Gln Arg Arg Gln Leu  
 35 40 45

Leu Gln Pro His Ala Leu Pro Gly Tyr Gly Cys Leu Leu His Asp His  
 50 55 60

Ala His Leu Leu His Pro His Gln Asp Glu Gly Gln  
 65 70 75

&lt;210&gt; 385

&lt;211&gt; 56

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 385

Trp Leu Leu Gln Ala Arg Val His His Leu Leu Leu Pro Val Arg Pro  
 1 5 10 15

Leu Gln Arg His Arg Pro Cys His Pro Gly His Pro Gly Pro Gly Pro  
 20 25 30

His Pro Pro Gly His Pro Leu Gly Ser Pro Leu Lys Pro Pro Arg Gln  
 35 40 45

Thr His Ser Arg Thr Lys Leu Ser  
 50 55

&lt;210&gt; 386

&lt;211&gt; 52

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

176

&lt;400&gt; 386

Gln Glu Phe Gln Thr Gly Leu Gly Asn Met Val Lys Pro Cys Leu Tyr  
1 5 10 15

Glu Lys Tyr Arg Asn Ile Ser Trp Leu Trp Trp His Thr Pro Val Val  
20 25 30

Pro Ala Thr Trp Glu Ala Glu Val Gly Gly Ser Leu Glu Pro Gly Arg  
35 40 45

Leu Arg Leu Gln  
50

&lt;210&gt; 387

&lt;211&gt; 65

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 387

Ile Leu Gly Gly Glu Ser Ile Leu Ile Leu Ser Trp Val Phe Ser Tyr  
1 5 10 15

Ile Phe Phe Arg Ile Ala Leu Glu Ile Thr Ile Tyr Ile Leu Asn Val  
20 25 30

Ser Pro Phe Cys Leu Gly Arg Trp Leu Met Pro Val Ile Pro Ala Leu  
35 40 45

Trp Glu Ala Glu Val Gly Gly Leu Pro Glu Leu Arg Ser Ser Arg Pro  
50 55 60

Ala  
65

&lt;210&gt; 388

&lt;211&gt; 15

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 388

Met Pro Lys Gln Leu Ala Gln Leu Leu Tyr Arg Leu Pro Arg Gly  
1 5 10 15

&lt;210&gt; 389

&lt;211&gt; 46

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 389

Leu Phe Gln Ala Ile Ser Val Ser Gly Ser His Arg Gln Gly Ser Arg  
1 5 10 15

Thr Trp Asn Thr Leu Thr Glu Gly Asn Ala Glu Ala Ala Cys Thr Val  
20 25 30

Ala Leu Gln Thr Ser Lys Arg Leu Ile Leu Ala Ser Arg Trp



177

35

40

45

&lt;210&gt; 390

&lt;211&gt; 50

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 390

Thr Leu Ser Phe Met Asn Ser His Cys Val Pro Ile Lys Ala Leu Phe  
 1 5 10 15

Phe Leu Ser Val Val Ser Tyr Ile Phe Ile Met Pro His His Ile Phe  
 20 25 30

Phe Thr Val Lys Ile Leu Lys Ser Cys Phe Gln Val Gly Gln Leu Met  
 35 40 45

Lys Leu  
 50

&lt;210&gt; 391

&lt;211&gt; 109

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 391

Arg Pro Thr Arg Pro Ile Thr Phe Ser Ser Asn Ile Ser Glu Trp Val  
 1 5 10 15

Pro Ser Thr Gly Phe Gln Asp Leu Glu His Phe Asn Arg Arg Lys Cys  
 20 25 30

Arg Ser Ser Leu His Ser Cys Phe Thr Asp Phe Gln Glu Ala Asp Ser  
 35 40 45

Gly Phe Lys Met Glu Pro Trp Ser Trp Phe Phe Phe Phe Phe Phe  
 50 55 60

Phe Pro Gln Arg Thr Cys Gly Cys Ala Leu Cys Val Leu Phe Leu Phe  
 65 70 75 80

Ser Ile Trp Gly Pro His Gly Lys Glu Leu Leu Asn Ser Phe Leu Tyr  
 85 90 95

Glu Leu Pro Leu Cys Ser Tyr Lys Gly Pro Phe Leu Ser  
 100 105

&lt;210&gt; 392

&lt;211&gt; 62

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 392

Val Asp Pro Arg Val Arg Leu Pro Leu Phe Trp Trp Gln Pro Ser Cys  
 1 5 10 15

Ala Val Tyr Leu Phe Pro Arg Val Tyr Asn Asn Met Cys Thr Arg Val

178

20 25 30  
 Leu Gly Thr Leu Pro His Cys Trp Asp Leu Ala Thr Leu Leu Gln Pro  
 35 40 45

Ser Ser Arg Ile Trp Gly Asn Val Ser Glu Ala Pro Gly Met  
 50 55 60

<210> 393  
 <211> 87  
 <212> PRT  
 <213> Homo sapiens

<400> 393  
 Val Pro Tyr His Ile Ala Gly Thr Leu Pro His Cys Cys Ser Leu Pro  
 1 5 10 15

Val Gly Tyr Gly Gly Met Ser Val Arg Leu Gln Gly Cys Arg Tyr Val  
 20 25 30

Gly Asn Val Gly Pro Gln Gly Asn Met Gln Ser Gly Arg Ser Trp Ala  
 35 40 45

Leu Lys Met Val Leu Leu Cys Asn Ser Cys Leu Gly Leu Gly Val Gly  
 50 55 60

Ser Val Gly Pro Ser Met Ser Ser Leu Phe Gly Ala Val Leu Ser Glu  
 65 70 75 80

Thr Pro Gly Ser Ser Val Tyr  
 85

<210> 394  
 <211> 29  
 <212> PRT  
 <213> Homo sapiens

<400> 394  
 Met Leu Asp Pro Arg Ala Thr Cys Asn Leu Val Gly Val Gly Leu Ser  
 1 5 10 15

Lys Trp Cys Cys Cys Val Thr Ala Ala Trp Val Leu Gly  
 20 25

<210> 395  
 <211> 65  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (48)  
 <223> Xaa equals any one of the naturally occurring L-amino acids

<400> 395  
 His Gly Asp Trp Ile Tyr Val His Ile Val Glu Gln Leu Asn Gln Ala  
 1 5 10 15

179

Asn Asn Lys Ser Val Thr Ser His Thr Tyr Phe Val Val Lys Thr Cys  
 20 25 30

Lys Ile His Ser Leu Ser Asn Phe Gln Ala Ser Asn Thr Leu Leu Xaa  
 35 40 45

Thr Val Val Thr Met Leu Tyr Asn Arg Ser Leu Glu Leu Ile Leu Pro  
 50 55 60

Val  
 65

<210> 396

<211> 68

<212> PRT

<213> Homo sapiens

<220>

<221> misc feature

<222> (26)

<223> Xaa equals any one of the naturally occurring L-amino acids

<400> 396

Thr Tyr Ser Ser Cys Leu Thr Lys Ile Leu Tyr Ser Leu Ile Asn Ile  
 1 5 10 15

Tyr Pro Ile Pro His Cys Ser Pro Ala Xaa Ile Thr Thr Ile Leu Leu  
 20 25 30

Ser Ala Ser Met Asn Leu Thr Phe Phe Phe Phe Arg Phe His Ile Cys  
 35 40 45

Glu Ile Ala Gln Tyr Leu Ser Phe Cys Ala Trp Leu Ile Ser Leu Asn  
 50 55 60

Ile Lys Ser Leu  
 65

<210> 397

<211> 33

<212> PRT

<213> Homo sapiens

<400> 397

Met Asn Leu Thr Phe Phe Phe Phe Arg Phe His Ile Cys Glu Ile Ala  
 1 5 10 15

Gln Tyr Leu Ser Phe Cys Ala Trp Leu Ile Ser Leu Asn Ile Lys Ser  
 20 25 30

Leu

<210> 398

<211> 58

<212> PRT

180

&lt;213&gt; Homo sapiens

&lt;400&gt; 398

Leu Val Cys Tyr Cys Ser Thr Lys Lys Glu Lys Lys Leu His Glu Ile  
1 5 10 15

Ala Ile Gln Gln Gly Gln Asn Trp Arg Trp Leu Leu Phe Tyr Lys Glu  
20 25 30

Ile Ser Val Pro Gly Phe Gln Ser Val Trp Cys Ser Tyr Lys Cys Leu  
35 40 45

Cys Val Val Trp Lys Ala Gly Glu Gly Gly  
50 55

&lt;210&gt; 399

&lt;211&gt; 36

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 399

Arg Arg Ser Cys Ser Gly Pro Pro Leu Val Asn Thr Ala Gly Lys Ile  
1 5 10 15

Leu Ser Ser Ser Pro Ala Lys Leu Ala Cys Lys Arg Thr Asp Phe His  
20 25 30

Ile Pro Ser Ile  
35

&lt;210&gt; 400

&lt;211&gt; 37

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 400

Arg Ala Ser Ile Leu Gly Ile Asp Asn Glu Arg Gly Cys His Phe Arg  
1 5 10 15

His Phe Asn Pro Leu Lys Glu Tyr Lys Arg Lys Lys Lys Glu Asn Lys  
20 25 30

Ser Phe Arg Ile Val  
35

&lt;210&gt; 401

&lt;211&gt; 77

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 401

Ser Lys Asn Lys Thr Arg Gly Gly Asp Trp Cys Val Thr Val Leu Arg  
1 5 10 15

Lys Arg Arg Lys Ser Phe Met Lys Ser Pro Phe Ser Lys Asp Arg Thr  
20 25 30

181

Gly Asp Gly Phe Ser Phe Thr Lys Lys Ser Leu Ser Gln Ala Phe Ser  
35 40 45

Leu Phe Gly Val His Thr Ser Val Cys Val Leu Cys Gly Arg Arg Gly  
50 55 60

Lys Ala Gly Glu Gly Gly Pro Val Gln Gly Pro Leu Trp  
65 70 75

&lt;210&gt; 402

&lt;211&gt; 55

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 402

Met Lys Ser Pro Phe Ser Lys Asp Arg Thr Gly Asp Gly Phe Ser Phe  
1 5 10 15

Thr Lys Lys Ser Leu Ser Gln Ala Phe Ser Leu Phe Gly Val His Thr  
20 25 30

Ser Val Cys Val Leu Cys Gly Arg Arg Gly Lys Ala Gly Glu Gly Gly  
35 40 45

Pro Val Gln Gly Pro Leu Trp  
50 55

&lt;210&gt; 403

&lt;211&gt; 24

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 403

Met Gly Glu Ser Glu Cys Tyr Arg Arg Leu Ser Gly Ala Ser Cys Thr  
1 5 10 15

Trp Thr Val His Val Asp Phe Ala  
20

&lt;210&gt; 404

&lt;211&gt; 33

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 404

Met His Cys Gly Thr Arg Val Trp Lys Thr Met Lys His Asp Tyr Phe  
1 5 10 15

Leu Leu Ala Cys Leu Ser Met Thr Ser Thr Gly Gly Ile Leu Cys Thr  
20 25 30

Leu

&lt;210&gt; 405

&lt;211&gt; 67

182

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 405

Ser Thr Leu Ser Leu Ile Pro Thr Ser Ser Ser Leu Ser Phe Trp Pro  
 1 5 10 15

Trp Cys Thr Ala Ile Ile Gly Ser Ile Phe Thr Tyr Cys Val Cys Val  
 20 25 30

Cys Val Cys Phe Val Val Met Asn Arg Thr Cys Tyr Leu Pro Asn Ser  
 35 40 45

Ile Ile Tyr His Asn Ser Lys Leu Ala Thr Ile Ile Asp Lys Ser Met  
 50 55 60

Thr Leu Ser  
 65

&lt;210&gt; 406

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 406

Met Trp Ile Leu Pro Lys Val Ser Leu Ile Cys Ile Val Glu Leu Gly  
 1 5 10 15

Tyr Gly Lys Pro  
 20

&lt;210&gt; 407

&lt;211&gt; 62

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 407

Met Ser Thr Gly Asp Gly Arg Asp Ala Glu Lys Gly Trp Pro Val Ser  
 1 5 10 15

Glu Glu Glu Asn Gln Arg Ser Val Tyr Pro Gly Tyr Pro Glu Cys Asp  
 20 25 30

Glu Arg Gln Ala Val Pro Gln His Cys Ala Ile Ala Ser Pro Ser Ser  
 35 40 45

Leu Gln Ser His His Pro Ala Ser Ala Cys Val Pro Arg Arg  
 50 55 60

&lt;210&gt; 408

&lt;211&gt; 38

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 408

Gln Gln Met Thr Leu Gly Thr Lys Ile Lys Trp Gly Gln Leu Gln Arg  
 1 5 10 15

Gly Gln Glu Ile Pro Thr Gly Asp Phe Thr Val Arg Asn Phe Met Arg  
                   20                  25                  30

Phe Ser Ile Ile Tyr Cys  
                   35

<210> 409

<211> 31

<212> PRT

<213> Homo sapiens

<220>

<221> misc feature

<222> (11)

<223> Xaa equals any one of the naturally occurring L-amino acids

<400> 409

Pro Phe Leu Phe Cys Ala Ser Arg Ile Arg Xaa Gln Gly Ile Gly Ile  
       1                  5                  10                  15

His Gly Gln Val Ala Cys Ser Ala Val Arg Met Tyr Asn Asn Arg  
                   20                  25                  30

<210> 410

<211> 45

<212> PRT

<213> Homo sapiens

<400> 410

Val Leu Cys Glu Glu Ala Gly Gln Lys Val Pro Ser Thr Pro Ser Trp  
       1                  5                  10                  15

Ser Ser Trp Thr Leu Gln Lys Arg Leu Arg Gly Ser Pro Ala Glu Ala  
                   20                  25                  30

Asn Cys Ser Pro Ser Phe Pro Ala Pro Pro Gly Lys Glu  
                   35                  40                  45

<210> 411

<211> 103

<212> PRT

<213> Homo sapiens

<400> 411

Met Ser Leu Ser Ala Leu Ala Cys Asp Phe Thr Pro Ile Gln Pro Trp  
       1                  5                  10                  15

Glu Trp Glu Glu Tyr Glu Gln Ile Thr Leu Gly Leu Thr Ala Pro Ser  
                   20                  25                  30

Asn Leu Leu Glu Ser Asn Tyr Leu Gly Gln Ala Ser Glu Cys Phe Val  
                   35                  40                  45

Arg Lys Leu Val Arg Arg Phe Pro Gln Leu Leu Pro Gly Pro Pro Gly  
                   50                  55                  60

184

His Cys Arg Lys Asp Leu Gly Asp Pro Gln Gln Arg Pro Ile Ala Leu  
65 70 75 80

Leu Pro Ser Leu Pro His Gln Glu Arg Asn Asn Val His Arg Leu Glu  
85 90 95

Ala Asp Ser Glu Val Asp Leu  
100

<210> 412

<211> 46

<212> PRT

<213> Homo sapiens

<400> 412

Cys Val Asp Phe Asp Glu Tyr Phe Ser Ser Trp Glu Pro Leu Leu Lys  
1 5 10 15

Met Met Phe Lys Gly Val Val Gly Gly Lys Met Lys Ala Trp Arg Arg  
20 25 30

Lys Lys Arg Arg Lys Pro Leu Pro Tyr Lys Ile His Ala Asp  
35 40 45

<210> 413

<211> 30

<212> PRT

<213> Homo sapiens

<400> 413

Met Met Phe Lys Gly Val Val Gly Gly Lys Met Lys Ala Trp Arg Arg  
1 5 10 15

Lys Lys Arg Arg Lys Pro Leu Pro Tyr Lys Ile His Ala Asp  
20 25 30

<210> 414

<211> 37

<212> PRT

<213> Homo sapiens

<400> 414

Leu Ile Ser Ser Val Asn Lys Thr Lys Gln Lys Arg Ser Asp Ala Thr  
1 5 10 15

Leu Ser His Lys His Asp Arg Leu Leu Asn His Phe Val Phe Phe Gly  
20 25 30

Asn Ser Tyr Asn Tyr  
35

<210> 415

<211> 127

<212> PRT

<213> Homo sapiens



185

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (95)

&lt;223&gt; Xaa equals any one of the naturally occurring L-amino acids

&lt;400&gt; 415

Ser Ser Lys Phe Pro Ser Asp Met Leu Leu Arg Ile Gln Gln Ile Ile  
 1 5 10 15

Tyr Cys His Lys Leu Thr Ile Ile Leu Thr Lys Trp Arg Asn Thr Ala  
 20 25 30

Arg His Lys Ser Lys Lys Lys Glu Asp Glu Leu Ile Leu Lys His Glu  
 35 40 45

Leu Gln Leu Lys Lys Trp Lys Asn Arg Leu Ile Leu Lys Arg Ala Ala  
 50 55 60

Ala Glu Glu Ser Asn Phe Pro Glu Arg Ser Ser Ser Glu Val Phe Leu  
 65 70 75 80

Val Asp Glu Thr Leu Lys Cys Asp Ile Ser Leu Leu Pro Glu Xaa Ala  
 85 90 95

Ile Leu Gln Val Cys Met Asn Ser Val Tyr Ile Ile Tyr Tyr Asn Leu  
 100 105 110

Pro Ser Val Val Val His Ala Cys Asn Pro Ser Cys Leu Gly Gly  
 115 120 125

&lt;210&gt; 416

&lt;211&gt; 11

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 416

Ser Leu Glu Ser Thr Asn Ala Ile Lys Ser Asn  
 1 5 10

&lt;210&gt; 417

&lt;211&gt; 19

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 417

Ile Arg Pro Asn Lys Asn Asp Gln Met Arg His Cys Leu Ile Asn Met  
 1 5 10 15

Ile Asp Tyr

&lt;210&gt; 418

&lt;211&gt; 37

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 418

186

Ile Thr Leu Cys Phe Leu Glu Thr Ala Ile Thr Ile Asn Ile Tyr Ser  
1 5 10 15

Asn Leu Val Asn Phe Leu Gln Ile Cys Tyr Cys Gly Tyr Asn Arg Ser  
20 25 30

Ser Ile Val Thr Ser  
35

<210> 419

<211> 31

<212> PRT

<213> Homo sapiens

<400> 419

Ile Ser Phe Arg Tyr Ala Ile Ala Asp Thr Thr Asp His Leu Leu Ser  
1 5 10 15

Gln Ala Asn His Tyr Pro Asn Lys Met Ala Glu Tyr Ser Lys Thr  
20 25 30

<210> 420

<211> 86

<212> PRT

<213> Homo sapiens

<220>

<221> misc feature

<222> (18)

<223> Xaa equals any one of the naturally occurring L-amino acids

<400> 420

Pro Gln Ile Lys Leu Leu Asn Ser Asp Ala Leu Gly Met Arg Thr Thr  
1 5 10 15

Ser Xaa Asp Leu Val Pro Cys Asn Gln Cys Phe Ile Pro Leu Pro Pro  
20 25 30

Ser Cys Asn Arg Ile Ala Ser Arg Lys Ala Val Asn Trp Lys Gln Gln  
35 40 45

Arg Leu Pro Ala Val Arg Gly Leu Leu Asn Asn Ala Pro His Arg Arg  
50 55 60

Pro Pro Thr Pro Arg Thr Pro Cys Val Phe Pro Ser Glu Gly Pro Lys  
65 70 75 80

Gly Tyr Gly Phe His Val  
85

<210> 421

<211> 39

<212> PRT

<213> Homo sapiens

<220>

<221> misc feature

&lt;222&gt; (5)

&lt;223&gt; Xaa equals any one of the naturally occurring L-amino acids

&lt;400&gt; 421

Glu Gln Leu Ala Xaa Ile Ser Cys Arg Val Ile Asn Val Ser Phe Arg  
 1 5 10 15

Cys Leu His His Val Ile Glu Ser Leu Pro Glu Arg Gln Leu Thr Gly  
 20 25 30

Ser Ser Arg Gly Ser Gln Pro  
 35

&lt;210&gt; 422

&lt;211&gt; 73

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (45)

&lt;223&gt; Xaa equals any one of the naturally occurring L-amino acids

&lt;400&gt; 422

Glu Asp Cys Ser Thr Met Pro Pro Ile Ala Ala Pro Pro Pro Leu Ala  
 1 5 10 15

Pro Leu Val Phe Ser Pro Leu Arg Gly Pro Arg Val Met Ala Phe Met  
 20 25 30

Ser Arg Cys Gly Asp Arg Gly Gly Arg Gly Arg Ser Xaa Ala Gly Arg  
 35 40 45

Gly Trp Pro Trp Ser Glu Ser Gly Val Ile Asn Ala His Pro Lys Lys  
 50 55 60

Arg Pro Cys Pro Gly Pro Met Leu Ser  
 65 70

&lt;210&gt; 423

&lt;211&gt; 48

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 423

Glu Phe Gly Thr Arg Arg Gln Trp Gly Thr Arg Cys Phe Pro Pro Leu  
 1 5 10 15

Val Gly Arg Lys Gln Ser Ala Leu Arg Arg Arg Glu Gly Lys Ala Arg  
 20 25 30

Ala Gly Arg Cys Cys Gly Lys Arg Ser Val Lys Ala Gly Phe Asp Ala  
 35 40 45

<210> 424  
<211> 42  
<212> PRT  
<213> Homo sapiens

<400> 424  
Ala Thr Val Pro Gly Ser Ile Tyr Asn Tyr Phe Tyr His Tyr Asn Ala  
1 5 10 15  
Gly Ala Leu Lys Pro Glu His Ala Ser Glu Ser Pro Arg Gly Leu Cys  
20 25 30  
Ala Gln Thr Ala Gly Pro Phe Pro Ser Phe  
35 40

<210> 425  
<211> 56  
<212> PRT  
<213> Homo sapiens

<400> 425  
Ile Arg His Glu Pro Pro Pro Arg Phe Lys Arg Phe Ser Cys Leu  
1 5 10 15  
Ser Leu Leu Ser Ser Trp Asp Tyr Arg Arg Ala Pro Pro His Val Ala  
20 25 30  
Ile Phe Cys Thr Leu Ser Arg Asp Gly Val Leu Pro His Trp Pro Gly  
35 40 45  
Trp Ser Gln Thr Pro Asp Leu Lys  
50 55

<210> 426  
<211> 72  
<212> PRT  
<213> Homo sapiens

<400> 426  
Ser Thr His Leu Gly Leu Pro Arg Cys Trp Asp Tyr Arg His Glu Pro  
1 5 10 15  
Leu Cys Leu Ala Pro Phe Thr Thr Ile Ser Ile Ile Ile Met Gln Gly  
20 25 30  
Leu Ser Asn Leu Ser Met Pro Gln Asn Pro Pro Glu Gly Cys Ala His  
35 40 45  
Arg Leu Leu Asp Leu Ser Pro Ala Ser Asp Ser Val Pro Pro Glu Trp  
50 55 60  
Gly Ser Lys Ile Ala Phe Glu Val  
65 70

<210> 427  
<211> 26  
<212> PRT

<213> Homo sapiens

<400> 427

Leu Arg Val Gly Gly Thr Ser Glu Asn Cys Cys Arg Gly Glu Cys Cys  
1 5 10 15

Gly Ser Val Cys Ile Pro Pro Gly Arg Leu  
20 25

<210> 428

<211> 46

<212> PRT

<213> Homo sapiens

<400> 428

Gly Leu Cys Met Val His Ser Leu Leu Thr Ser Ser Leu Gly Gly Arg  
1 5 10 15

Cys Cys Asn Tyr Pro Tyr Ile Ala Asp Lys Asp Ile Glu Thr Glu Val  
20 25 30

Lys Pro Pro Ser Gln Gly His Thr Trp His Leu His Cys Ser  
35 40 45

<210> 429

<211> 75

<212> PRT

<213> Homo sapiens

<400> 429

Gln Leu Trp Cys Ile Thr Ala Leu Pro Ser Thr Arg His Cys Ser Lys  
1 5 10 15

Gly Phe Ala Trp Phe Thr His Ser Leu Arg His Pro Ser Val Ala Gly  
20 25 30

Ala Val Ile Ile Leu Ile Leu Gln Thr Arg Thr Leu Arg Gln Arg Ser  
35 40 45

Ser His Leu Pro Lys Gly Thr His Gly Ile Cys Thr Ala Pro Asp Arg  
50 55 60

Pro Thr Glu Arg Ala Ala Val Thr Ile Leu Lys  
65 70 75

<210> 430

<211> 39

<212> PRT

<213> Homo sapiens

<400> 430

Ser Phe Asp Asn Asn Asn Ser Tyr Gly Val Ser Gln Leu Tyr Gln Val  
1 5 10 15

Pro Asp Thr Val Leu Arg Ala Leu His Gly Ser Leu Thr Pro Tyr Val  
20 25 30

Ile Pro Arg Trp Gln Val Leu  
35

<210> 431  
<211> 38  
<212> PRT  
<213> Homo sapiens

<400> 431  
Asp Arg Gly Gln Ala Thr Phe Pro Arg Ala His Met Ala Ser Ala Leu  
1 5 10 15

Leu Leu Thr Asp Arg Gln Arg Glu Leu Leu Ser Arg Ser Ser Asn Glu  
20 25 30

Leu Cys Met Ser Lys Val  
35

<210> 432  
<211> 73  
<212> PRT  
<213> Homo sapiens

<220>  
<221> misc feature  
<222> (66)  
<223> Xaa equals any one of the naturally occurring L-amino acids

<400> 432  
Leu Leu Leu Ile Leu Arg Pro Phe Leu Asn Ser Gln Phe Lys Leu Gln  
1 5 10 15

Leu Pro Leu Val Leu Phe His Ser Ser Cys Thr Tyr Ile Cys Leu Leu  
20 25 30

Tyr Asn Tyr Glu Leu Phe His Ile Val Ala Leu Thr Gly Lys Leu Met  
35 40 45

Asn Leu Gly Leu His Leu Phe Ala His His Leu Ile Leu Ala Val Ala  
50 55 60

His Xaa Gly Cys Ser Ile Pro Ile Tyr  
65 70

<210> 433  
<211> 37  
<212> PRT  
<213> Homo sapiens

<400> 433  
Thr His Asn Ser Asn Tyr Ser Ser Leu Trp Phe Ser Ser Thr Ala Val  
1 5 10 15

Val Leu Thr Tyr Val Tyr Tyr Ile Ile Met Asn Cys Phe Ile Leu Ser  
20 25 30

Pro Leu Gln Val Asn

35

&lt;210&gt; 434

&lt;211&gt; 53

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 434

Thr Leu Val Ala Gly Ser Pro Cys Ser Leu Ser Arg Trp Ile Met Ala  
 1 5 10 15

Gly Phe Cys His Gly Glu Leu Val Gln Ser Asp Met Glu Ser Gln Glu  
 20 25 30

Trp Glu Arg Gly Gln Val Val Leu Ser His Thr Ser Leu Pro Trp Cys  
 35 40 45

Tyr Val Ser Pro Arg  
 50

&lt;210&gt; 435

&lt;211&gt; 39

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 435

Met Ala Gly Phe Cys His Gly Glu Leu Val Gln Ser Asp Met Glu Ser  
 1 5 10 15

Gln Glu Trp Glu Arg Gly Gln Val Val Leu Ser His Thr Ser Leu Pro  
 20 25 30

Trp Cys Tyr Val Ser Pro Arg  
 35

&lt;210&gt; 436

&lt;211&gt; 94

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 436

Met Ala Val Trp Ile Ser Gly Ser Tyr Ser Ser Phe Cys Ser Arg Ser  
 1 5 10 15

Asn Trp Asp Val Phe Ser Pro Asn Ile Val Leu Ala Ser Leu Pro Phe  
 20 25 30

Ser Phe Arg Ser Val Ser Lys Ala Ala Lys Pro Trp Trp Leu Ala Leu  
 35 40 45

Pro Ala Leu Phe Pro Asp Gly Leu Trp Leu Asp Ser Ala Met Gly Ser  
 50 55 60

Leu Tyr Ser Gln Thr Trp Lys Ala Arg Asn Gly Lys Glu Val Arg Trp  
 65 70 75 80

Phe Ser Pro Thr Pro His Cys Leu Gly Ala Met Ser His Leu

85

90

&lt;210&gt; 437

&lt;211&gt; 82

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 437

Arg Ser Lys Arg Gln Ser Gln Gly Ser Arg Cys Ser Val Pro Leu Leu  
 1 5 10 15

Ala Gln Gln Ser Arg Ser Pro Pro Val Pro Leu Gln Ala Gln Pro Ala  
 20 25 30

Trp Leu Leu Gly Ser Glu Thr Ile Ala Trp Ser Gly Gly Gly Ser Gly  
 35 40 45

Trp Glu Gly Pro Arg Asp Pro Gly Thr Ser Thr Ala Ala Gly Asn Ser  
 50 55 60

Gly Pro Gly Ile Gly Met Gly His Arg Thr Pro Pro Pro Ser His Thr  
 65 70 75 80

Gly Arg

&lt;210&gt; 438

&lt;211&gt; 30

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 438

Arg Trp Asp Pro Ala Trp Gly Leu Asp Ile Pro Glu Ser Ser Cys Pro  
 1 5 10 15

Val Thr Met Gly Glu Leu Arg Ser Gly Asp Gly Ile Val Leu  
 20 25 30

&lt;210&gt; 439

&lt;211&gt; 50

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 439

Gly Ala Leu Leu Trp Asp Asn Ser Met Ile Ser Ala Pro Arg Gly Ser  
 1 5 10 15

His Arg Glu Ala Gly Ala Leu Phe Pro Ser Trp Leu Ser Asn Pro Ala  
 20 25 30

Val Leu Pro Ser Arg Ser Arg Pro Ser Gln Pro Gly Cys Leu Asp Pro  
 35 40 45

Arg Gln

50



<210> 440  
 <211> 49  
 <212> PRT  
 <213> Homo sapiens

<400> 440  
 Asn Ser Ala Arg Glu Pro Arg Arg Trp Ile Arg Pro Thr Arg Gly Ser  
 1 5 10 15  
 Gly Glu Thr Thr Ala Pro Cys Cys Phe Glu Pro Leu Asn Gly Gly Thr  
 20 25 30  
 Leu Val His Ala Ala Ala Met Ala Arg Ala Ser Glu Ala Ala Gly Thr  
 35 40 45

Gly

<210> 441  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 441  
 Met Ala Arg Ala Ser Glu Ala Ala Gly Thr Gly  
 1 5 10

<210> 442  
 <211> 84  
 <212> PRT  
 <213> Homo sapiens

<400> 442  
 Cys Phe Thr Thr Ala Phe Gln Lys Ala Leu Arg Asp Pro Arg Pro Thr  
 1 5 10 15  
 Leu Pro Asp Thr His Gly Ser Leu Arg Asn Ala Pro Leu Lys Ser Leu  
 20 25 30  
 Thr Leu Pro Ala Ala Phe Val Val Ser Phe Phe Phe Leu Ser Leu Leu  
 35 40 45  
 Gln Asp Gly Ile Lys Glu Arg Ser Gln Thr Gln Asn Ala Thr Phe Phe  
 50 55 60  
 Phe His Asp Arg Ser Asp Ile Glu Gly Leu Ser Glu Glu Pro Cys Ser  
 65 70 75 80

Gly Thr Thr Pro

<210> 443  
 <211> 95  
 <212> PRT  
 <213> Homo sapiens

<400> 443

194

Leu Ala Leu Gln Glu Ala Val Thr Gly Lys Gln Val Leu Cys Ser Pro  
 1 5 10 15  
 Pro Gly Ser Ala Ile Pro Gln Ser Ser Arg Pro Ala Pro Gly Pro Ala  
 20 25 30  
 Ser Leu Ala Ala Trp Ile Arg Asp Asn Ser Leu Val Trp Arg Arg Leu  
 35 40 45  
 Arg Val Gly Gly Thr Gln Gly Pro Gly His Gln Tyr Ser Ser Trp Glu  
 50 55 60  
 Phe Arg Pro Arg Asp Arg Asp Gly Ala Gln Asp Thr Thr Pro Ile Ser  
 65 70 75 80  
 His Arg Glu Met Lys Val Gly Ser Ser Met Gly Thr Gly His Pro  
 85 90 95

<210> 444  
 <211> 42  
 <212> PRT  
 <213> Homo sapiens

<400> 444  
 Met Phe Tyr Ser Lys Ile Phe Tyr Phe Leu Leu Leu Asn Ser Asp Thr  
 1 5 10 15  
 Ser Asn Asn Val Thr Ser Lys Thr Leu Val Ser Ser Ile Ser Ser Ser  
 20 25 30  
 Asn Asn Arg Leu Ala Val Ser Ile Val Phe  
 35 40

<210> 445  
 <211> 47  
 <212> PRT  
 <213> Homo sapiens

<400> 445  
 Ser Arg Gln Lys Asn Leu Leu Lys Leu His Ser Asn Pro Asn Cys Asp  
 1 5 10 15  
 Asn Phe Cys Phe Ile Phe Asn Tyr Lys Pro Lys Tyr Ile Cys Ile Phe  
 20 25 30  
 Lys Leu Ile Cys Leu Lys Ile Leu Leu Tyr Ile Phe Gly Ser Gly  
 35 40 45

<210> 446  
 <211> 56  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <222> (24)  
 <223> Xaa equals any one of the naturally occurring L-amino acids

&lt;400&gt; 446

Met Leu Leu Ser Leu Leu Met Val Phe Thr Ser Glu Leu Tyr Val Lys  
 1 5 10 15

Arg His Ile Ser Phe Lys Ser Xaa Asp Lys Pro His Cys His Lys Asn  
 20 25 30

Gln Asp Ile Asp Val Leu Phe Arg Lys Leu Leu Glu Lys His Phe Lys  
 35 40 45

Val Ile Asn Met Ile Cys Phe Pro  
 50 55

&lt;210&gt; 447

&lt;211&gt; 12

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 447

Phe Arg Glu Tyr Gly Phe Tyr Asn Leu His Phe Cys  
 1 5 10

&lt;210&gt; 448

&lt;211&gt; 38

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 448

Leu Val Thr Thr Asp Tyr Tyr Asp Gly Cys Asn Glu Asp Tyr Glu Tyr  
 1 5 10 15

Asn Trp Ser Tyr Met Phe Leu Asn Ser Glu Gln Leu Phe Ile Lys Phe  
 20 25 30

Tyr Pro Thr Phe Phe Cys  
 35

&lt;210&gt; 449

&lt;211&gt; 52

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 449

Asn Val Ile Ala Pro Gly Leu Glu Ser Ser Cys Ala Asn Ser Leu Phe  
 1 5 10 15

Leu Leu Phe Val Cys Leu Pro Val Ala His His Arg His Asn Phe Leu  
 20 25 30

Phe Ile Lys His Ser Leu Tyr Asn His Leu Arg Asp Tyr Glu Ser Asp  
 35 40 45

Phe Asp Lys Ile  
 50

<210> 450  
 <211> 34  
 <212> PRT  
 <213> Homo sapiens

<400> 450  
 Pro Lys Val Leu Ala Val Leu Lys Lys Lys Asn His Val Ala Leu Ser  
 1 5 10 15

Ile Phe Glu Leu Leu Ser Asn Asp Ile Cys Ser Phe Ile Ser Phe Phe  
 20 25 30

Met Ser

<210> 451  
 <211> 28  
 <212> PRT  
 <213> Homo sapiens

<400> 451  
 Glu Gly Pro Asp Ile Asn Ser Asn Leu Lys Phe Leu Leu Cys Leu Lys  
 1 5 10 15

Lys Lys Ile Met Trp Pro Phe Gln Tyr Leu Asn Cys  
 20 25

<210> 452  
 <211> 47  
 <212> PRT  
 <213> Homo sapiens

<400> 452  
 Leu Leu Ser Leu Ile Leu Leu Arg Ile Trp Tyr Asp Phe Ser Lys Gln  
 1 5 10 15

Thr Val Phe Trp Phe Phe Leu Asn Val Phe Asn Phe Phe Ser Ser Cys  
 20 25 30

Asn Asn Asp Gly Ala Cys Ser Tyr Lys Tyr Arg Lys Val Gln Ile  
 35 40 45

<210> 453  
 <211> 12  
 <212> PRT  
 <213> Homo sapiens

<400> 453  
 His Thr Leu Phe Ile Ser Phe Leu Trp Ala Glu Gly  
 1 5 10

<210> 454  
 <211> 28  
 <212> PRT  
 <213> Homo sapiens

&lt;400&gt; 454

Met Leu Pro Val Phe Val Leu Phe Phe Cys Phe Thr Tyr Ser Ala Arg  
 1 5 10 15

Lys Gln Ser Val Phe Lys Lys Gly Asn Val Phe Glu  
 20 25

&lt;210&gt; 455

&lt;211&gt; 63

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 455

Ser Pro Cys Ser Ala Ala Glu Cys His Asn Leu Ser Leu Leu Ser Ser  
 1 5 10 15

Cys Ser Leu Val Ser Ser Asn Ile Leu Phe Ser Phe Pro Phe Phe Gly  
 20 25 30

Gln Lys Ala Arg Cys Cys Leu Phe Leu Phe Tyr Phe Ser Ala Ser His  
 35 40 45

Ile Ala His Glu Ser Arg Val Tyr Ser Lys Lys Glu Met Cys Leu  
 50 55 60

&lt;210&gt; 456

&lt;211&gt; 65

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 456

His Lys Cys Phe Gln Cys Phe Ile Leu Ala Asn Gly Phe Leu Lys Val  
 1 5 10 15

Ile Lys Pro Phe Gln Arg Asn Trp Ser Asp Lys Thr Phe Phe Leu Val  
 20 25 30

Cys Leu Asn Lys Ala Ile Ser Glu Ala Leu Leu Ser Lys Met Thr Phe  
 35 40 45

Leu Ser Phe Phe Lys Thr Asn Leu Leu Leu Leu Glu Thr Phe Cys Thr  
 50 55 60

Ile

65

&lt;210&gt; 457

&lt;211&gt; 99

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 457

Leu Leu Gly Val Leu Lys Pro Leu Tyr Phe Ser Val Glu Pro Val Leu  
 1 5 10 15

Gly Glu Arg Ser Val Ala Phe Glu Glu Val Arg Glu Lys Asn His Gly  
 20 25 30

Thr Ser Gly Phe Leu Ser Leu Tyr Ser Leu Ala Ala Ile Val Cys Gly  
35 40 45

His Leu Met Phe Phe His Thr Leu Leu Gly Arg Gly Gly Asn Asp His  
50 55 60

Pro Gly Gln Ser Pro Leu Pro Gly Met Arg Pro Leu Arg Gly Gly Leu  
65 70 75 80

Ala Gly Gln Ala Pro Ser Gly His Pro Trp Met Gln Pro Leu Asp Thr  
85 90 95

Cys Leu Leu

<210> 458

<211> 43

<212> PRT

<213> Homo sapiens

<400> 458

Arg Pro Thr Arg Pro Thr Arg Pro Asp Arg Pro Ser Leu Glu Leu  
1 5 10 15

Ala Pro Gly Leu Cys Ala Asp Phe Leu Gly Ser Ser Asn His Cys Ile  
20 25 30

Phe Leu Leu Ser Leu Tyr Leu Gly Arg Asp Gln  
35 40

<210> 459

<211> 49

<212> PRT

<213> Homo sapiens

<400> 459

Glu Lys Arg Ile Met Val Pro Gln Gly Phe Phe Pro Phe Thr Arg Trp  
1 5 10 15

Gln Pro Leu Ser Val Gly Thr Ser Cys Phe Ser Thr Leu Tyr Trp Ala  
20 25 30

Val Glu Val Thr Ile Thr Gln Ala Ser Leu Leu Cys Leu Gly Cys Ala  
35 40 45

Leu

<210> 460

<211> 123

<212> PRT

<213> Homo sapiens

<400> 460

Met Thr Leu Asp Glu Trp Lys Asn Leu Gln Glu Gln Thr Arg Pro Lys  
1 5 10 15

Pro Glu Phe Asn Ile Arg Lys Pro Glu Ser Thr Val Pro Ser Lys Ala  
 20 25 30

Val Val Ile Arg Glu Ser Lys Tyr Arg Asp Asp Met Val Lys Asp Asp  
 35 40 45

Tyr Glu Asp Asp Ser His Val Phe Arg Lys Pro Ala Asn Asp Ile Thr  
 50 55 60

Ser Gln Leu Glu Ile Asn Phe Gly Asn Leu Pro Arg Pro Gly Arg Gly  
 65 70 75 80

Ala Arg Gly Gly Thr Arg Gly Gly Arg Gly Arg Ile Arg Arg Ala Glu  
 85 90 95

Asn Tyr Gly Pro Arg Ala Glu Val Val Met Gln Asp Val Ala Pro Asn  
 100 105 110

Pro Asp Asp Pro Glu Asp Phe Pro Ala Leu Ser  
 115 120

<210> 461  
 <211> 100  
 <212> PRT  
 <213> Homo sapiens

<400> 461  
 Cys Lys Met Leu Pro Pro Thr Gln Met Thr Arg Lys Ile Ser Leu Arg  
 1 5 10 15

Cys Leu Glu Arg Ala Leu Phe Pro Ser Thr Ala Glu Leu His Cys Thr  
 20 25 30

Pro Val Gly Arg Leu Phe Gln Leu Gly Gln Gly Ser Gln Thr Leu Arg  
 35 40 45

Thr Ile Asp Val Ala Phe Pro Val Ser Cys Lys Phe Val Ala Leu Phe  
 50 55 60

Trp Ala Glu Leu Leu Glu Gly Leu Leu Gln Arg Leu Glu Ser Arg Pro  
 65 70 75 80

Phe Pro Lys Lys Met Lys Asn Gly Asp Cys Val Phe Ile Glu Gly Ile  
 85 90 95

Ser Asn Glu Glu  
 100

<210> 462  
 <211> 41  
 <212> PRT  
 <213> Homo sapiens

<400> 462  
 Pro Pro Ser Ser Trp Ala Trp Ser Gln Arg Arg His Pro Gly Arg Pro  
 1 5 10 15

200

Gly Lys Asp Gln Glu Gly Arg Glu Leu Trp Thr Gln Ser Arg Ser Gly  
                   20                  25                  30

Asp Ala Arg Cys Cys Pro Gln Pro Arg  
           35                  40

<210> 463  
 <211> 22  
 <212> PRT  
 <213> Homo sapiens

<400> 463  
 Cys Leu Lys Cys Val Tyr Arg Asp Ser Ile Asp Ser Ser Ala Glu Ala  
       1                  5                  10                  15

Trp Arg Glu Arg Arg Leu  
           20

<210> 464  
 <211> 29  
 <212> PRT  
 <213> Homo sapiens

<400> 464  
 Leu Ser Tyr Ser Val Leu Leu Ile Leu Pro Leu Phe His Ser Leu Pro  
       1                  5                  10                  15

Thr Leu Lys Asp Thr His Thr His Asn Lys Trp Val Glu  
                   20                  25

<210> 465  
 <211> 61  
 <212> PRT  
 <213> Homo sapiens

<400> 465  
 Glu Val Asn Gly Val Gly Tyr Lys His Ser Cys Phe Ser Asp Ile Ser  
       1                  5                  10                  15

Ser Val Leu Glu Asn Lys Asp Ser Arg Met Arg Ala Pro His Tyr Ala  
                   20                  25                  30

Ser Phe Gln His Phe Phe Ser Val Leu Leu Lys Leu Ser Pro Gln Ala  
           35                  40                  45

Cys Leu Thr Glu Ser Gln Cys Ile Pro Leu Thr Phe Tyr  
       50                  55                  60

<210> 466  
 <211> 37  
 <212> PRT  
 <213> Homo sapiens

<400> 466  
 Lys Thr His Thr His Thr Ile Ser Gly Trp Ser Lys Lys Ser Thr Glu  
       1                  5                  10                  15



201

Leu Asp Ile Ser Ile Pro Ala Phe Leu Thr Ser Pro Val Ser Trp Arg  
 20 25 30

Thr Arg Ile Leu Glu  
 35

&lt;210&gt; 467

&lt;211&gt; 29

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 467

Ile Arg His Glu Leu Gly Ser Ser Asp Pro Pro Ala Glu Ala Ser Gln  
 1 5 10 15

Ile Ala Gly Thr Ala Ala Val Ser His His Ala Gln Pro  
 20 25

&lt;210&gt; 468

&lt;211&gt; 25

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 468

Met Leu Tyr Leu Ile Leu Ile Ser Leu Ser Ser Leu Ser Phe Ser Phe  
 1 5 10 15

Ser Leu Pro Pro Phe Ser Ile Ile Ile  
 20 25

&lt;210&gt; 469

&lt;211&gt; 24

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 469

Ser Ser Tyr Phe Leu Arg His Phe Arg Ile Tyr His Thr Cys Pro Lys  
 1 5 10 15

Tyr Phe Ser Met Asn Ile Ile Asn  
 20

&lt;210&gt; 470

&lt;211&gt; 69

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 470

Lys Leu Thr Leu Thr Lys Gly Asn Lys Ser Trp Ser Ser Thr Ala Val  
 1 5 10 15

Ala Ala Ala Leu Glu Leu Val Asp Pro Pro Gly Cys Arg Asn Ser Ala  
 20 25 30

Arg Asp Ser Leu Pro Asn Ser Thr Met Met Phe Tyr Tyr Ala Cys Phe

202

35 40 45  
 Ile Leu Tyr Ser Ser Leu Ser Pro Leu Ser Leu Ser Leu Ser Pro Ser  
 50 55 60

Leu Leu Ser Leu Leu  
 65

<210> 471  
 <211> 14  
 <212> PRT  
 <213> Homo sapiens

<400> 471  
 Gln Phe His Thr Gly Asn Ser Tyr Asp His Asp Tyr Ala Lys  
 1 5 10

<210> 472  
 <211> 35  
 <212> PRT  
 <213> Homo sapiens

<400> 472  
 Ala Val Cys Thr Gly Gly Tyr Cys Glu Ser Cys Arg Cys Glu His Cys  
 1 5 10 15

Val Cys Val Cys Val Asp Leu Cys Val Leu Phe Ser Gly Lys Glu Leu  
 20 25 30

Arg Val Arg  
 35

<210> 473  
 <211> 72  
 <212> PRT  
 <213> Homo sapiens

<400> 473  
 Val Ser Phe Phe Phe Val Phe Lys Trp Ser Phe Ala Glu Ile Lys Ser  
 1 5 10 15

Arg Glu Glu His Trp Ala Ser Leu Thr Pro Lys Pro Thr Leu Leu Ser  
 20 25 30

Ala Leu Leu Thr Cys Asp Val Leu Lys Ser Ser Ile Ile Phe Lys Cys  
 35 40 45

Cys Glu Ser Thr Glu Asp Lys Gly Phe Asp Ser Phe Phe Gln Ala Ser  
 50 55 60

Lys Asp Gly Ser Ser Ser Arg Ile  
 65 70

<210> 474  
 <211> 99  
 <212> PRT

203

&lt;213&gt; Homo sapiens

&lt;400&gt; 474

Arg Ser Trp Gly Ser Gln Arg Ser Leu Cys Leu Leu Phe Ile Pro Phe  
 1 5 10 15  
 Ala Ala Glu Ser Tyr Ser Val Val Trp Met Gly His Leu Phe Val Val  
 20 25 30  
 Cys Leu Leu Ser Ser Trp Trp Thr Phe Arg Pro Phe Ala Leu Ala Val  
 35 40 45  
 Thr Val Asn His Val Ala Val Asn Ile Val Cys Val Ser Ala Trp Thr  
 50 55 60  
 Cys Val Ser Cys Ser Leu Gly Arg Ser Cys Gly Leu Glu Gly Ser Phe  
 65 70 75 80  
 Leu Phe Pro Leu Glu Thr Leu Trp Phe Pro His Met Val Val Leu Cys  
 85 90 95  
 Leu Thr Phe

&lt;210&gt; 475

&lt;211&gt; 74

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 475

Met Gly His Leu Phe Val Val Cys Leu Leu Ser Ser Trp Trp Thr Phe  
 1 5 10 15  
 Arg Pro Phe Ala Leu Ala Val Thr Val Asn His Val Ala Val Asn Ile  
 20 25 30  
 Val Cys Val Ser Ala Trp Thr Cys Val Ser Cys Ser Leu Gly Arg Ser  
 35 40 45  
 Cys Gly Leu Glu Gly Ser Phe Leu Phe Pro Leu Glu Thr Leu Trp Phe  
 50 55 60  
 Pro His Met Val Val Leu Cys Leu Thr Phe  
 65 70

&lt;210&gt; 476

&lt;211&gt; 51

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 476

His Asp Val Leu Gly Ala Arg Asn Ala Ala Cys Val Cys Cys Ser Phe  
 1 5 10 15  
 Leu Leu Gln Gln Asn Arg Ile Leu Leu Phe Gly Trp Ala Thr Cys Leu  
 20 25 30  
 Leu Ser Val Tyr Ser Pro Ala Gly Gly His Leu Gly Arg Leu His Trp

204

35                      40                      45  
 Arg Leu Leu  
 50  
  
 <210> 477  
 <211> 130  
 <212> PRT  
 <213> Homo sapiens  
  
 <400> 477  
 Met Leu Asp Phe Lys Thr Ser Gln Val Ser Lys Ala Leu Lys Arg Val  
 1                      5                      10                      15  
 Gly Phe Gly Val Arg Leu Ala Gln Cys Ser Ser Leu Asp Leu Ile Ser  
                     20                      25                      30  
 Ala Lys Leu His Leu Lys Thr Lys Lys Lys Glu Thr Tyr Ile Thr Ser  
                     35                      40                      45  
 Thr Val Met Thr Ala Ala Ser Leu Phe Leu Ser Tyr Val Thr Ser Glu  
                     50                      55                      60  
 Phe Thr Arg Ser Ile Met Ala Thr Phe Tyr Cys Phe Val Leu Lys Leu  
                     65                      70                      75                      80  
 His Ile Gly Glu Met Gly Thr Leu Gln Thr Ala Gly Gly Ser Lys Met  
                     85                      90                      95  
 Thr Trp Pro Leu Gln Lys Ala Ile Trp Gln Phe Leu Lys Arg Leu Ser  
                     100                      105                      110  
 Ile Lys Leu Pro Tyr Val Glu Thr Arg Glu Ser Pro Gly Glu Thr Lys  
                     115                      120                      125  
  
 Asn Tyr  
 130

<210> 478  
 <211> 28  
 <212> PRT  
 <213> Homo sapiens

<400> 478  
 Leu Thr Arg Asn Ser Phe Pro Glu Asn Arg Thr His Lys Ser Thr Gln  
 1                      5                      10                      15  
 Thr His Thr Gln Cys Ser Gln Arg His Asp Ser Gln  
                     20                      25

&lt;210&gt; 479

&lt;211&gt; 90

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 479

Ile Arg His Glu Gly Gln Ser Ser Ser Arg Gly Ser Ser His Cys Asp  
 1 5 10 15

Ser Pro Ser Pro Gln Glu Asp Gly Gln Ile Met Phe Asp Val Glu Met  
 20 25 30

His Thr Ser Arg Asp His Ser Ser Gln Ser Glu Glu Glu Val Val Glu  
 35 40 45

Gly Glu Lys Glu Val Glu Ala Leu Lys Lys Ser Ala Asp Trp Val Ser  
 50 55 60

Asp Trp Ser Ser Arg Pro Glu Asn Ile Pro Pro Lys Glu Phe His Phe  
 65 70 75 80

Arg His Pro Lys Arg Ser Val Ser Leu Ser  
 85 90

&lt;210&gt; 480

&lt;211&gt; 40

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 480

Gly Ile Leu Leu Thr Leu Tyr Pro Phe Trp Pro Glu Asp Ile Leu Glu  
 1 5 10 15

Phe Pro Asn Arg Val Tyr Cys Cys Leu Glu Ile Cys Lys Gly Phe Phe  
 20 25 30

Ser Ala Asn Ala Thr Ser Arg Leu  
 35 40

206

<210> 481  
<211> 47  
<212> PRT  
<213> Homo sapiens

<400> 481  
Glu Phe Gly Thr Arg Asp Arg Val Val Pro Glu Ala Val Leu Thr Val  
1 5 10 15  
Thr Ala Leu Arg His Lys Lys Met Gly Arg Ser Cys Leu Met Trp Lys  
20 25 30  
Cys Thr Pro Ala Gly Thr Ile Ala Leu Ser Gln Lys Lys Lys Leu  
35 40 45

<210> 482  
<211> 52  
<212> PRT  
<213> Homo sapiens

<400> 482  
Ala His Pro Leu Pro Ala Pro Thr Glu Gly Lys Glu Lys Pro Leu Glu  
1 5 10 15  
Met Arg Val Thr Cys Glu Val Val Tyr Cys His Ser Ser Leu Phe Glu  
20 25 30  
Leu Glu Thr Ile Val Ser Met Thr Gln Pro Thr Thr Leu Phe Leu His  
35 40 45  
Ile Gln Phe Gln  
50

<210> 483  
<211> 68  
<212> PRT  
<213> Homo sapiens

<400> 483  
Thr Phe Cys Val Phe Lys His Glu Glu Lys Trp Ser His Glu Glu Arg  
1 5 10 15  
Gly Tyr Phe Leu Arg Arg Ile Ser Glu Gly Val His Ser Ile Ser Leu  
20 25 30  
Pro Phe Ser Cys Phe Gly Phe Gly Ala Arg His Leu Tyr Trp Lys Ala  
35 40 45  
Thr Glu His Thr Leu Cys Gln His Leu Leu Arg Glu Arg Lys Ser Pro  
50 55 60  
Trp Lys Cys Val  
65

&lt;210&gt; 484

&lt;211&gt; 64

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 484

Gln Ser Leu Leu Leu Phe Arg Asn Leu Gln Gly Leu Leu Phe Arg Lys  
1 5 10 15

Cys His Gln Gln Ile Ile Ile Leu Ser Ala Met Leu Leu Ser Leu Ile  
20 25 30

Ser Ala Thr Arg Leu Asp Leu Tyr His Ser Trp Tyr Lys Phe Tyr Ser  
35 40 45

Cys Asn Ile Thr Thr Ile Ser Leu Leu Lys Arg Asp Gln Val Ser Lys  
50 55 60

&lt;210&gt; 485

&lt;211&gt; 22

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 485

Ile Arg His Glu Glu Ser Phe Asn Pro Leu Thr Cys Gly Phe Ser Leu  
1 5 10 15

Phe Phe Ser Leu Phe Ser  
20

&lt;210&gt; 486

&lt;211&gt; 27

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 486

Met Glu Thr Leu Leu Leu Leu Phe Phe Leu Ser Leu Leu Ile Phe  
1 5 10 15

Arg Phe Arg Ile Leu Val Ser Gln Cys Ile Asn  
20 25

<210> 487  
 <211> 65  
 <212> PRT  
 <213> Homo sapiens

<400> 487  
 Phe Leu Leu Thr Thr Val Leu Leu Phe Ser Ser Lys Val Arg Asp Pro  
 1 5 10 15  
 Arg Ala Asn Phe Asp Gln Ser Leu Arg Val Leu Lys His Ala Lys Lys  
 20 25 30  
 Val Gln Pro Asp Val Ile Ser Lys Thr Ser Ile Met Leu Gly Leu Gly  
 35 40 45  
 Glu Asn Asp Glu Gln Val Tyr Ala Thr Met Lys Gly Lys Glu Ile Glu  
 50 55 60  
 Lys  
 65

<210> 488  
 <211> 23  
 <212> PRT  
 <213> Homo sapiens

<400> 488  
 Gln Gln Ser Cys Cys Phe Pro Val Arg Phe Val Ile Leu Gly Pro Ile  
 1 5 10 15  
 Leu Ile Ser Pro Tyr Val Tyr  
 20

<210> 489  
 <211> 59  
 <212> PRT  
 <213> Homo sapiens

<400> 489  
 Val Trp Leu Leu Ser Ser Ile Leu Leu Arg Val Leu Trp Asn Arg Tyr  
 1 5 10 15  
 Thr Leu Gln Glu Leu Ser Phe Trp Leu Pro Trp Phe Ala Ser Arg Ala  
 20 25 30  
 Thr Ser Leu Val Leu Gln His Gly Asp Asn Tyr Leu Leu Phe Leu Phe  
 35 40 45  
 Cys Phe Val Cys Phe Val Leu Ala Met Pro Phe  
 50 55



209

<210> 490  
<211> 26  
<212> PRT  
<213> Homo sapiens

<400> 490  
Ile Arg His Glu Val Ser Met Ala Phe Val Phe His Leu Ala Gln Gly  
1 5 10 15  
Thr Leu Glu Pro Leu Tyr Ile Ala Gly Ala  
20 25

<210> 491  
<211> 40  
<212> PRT  
<213> Homo sapiens

<400> 491  
Asn Ser Ala Arg Gly Glu Tyr Gly Phe Cys Leu Pro Ser Cys Ser Gly  
1 5 10 15  
Tyr Phe Gly Thr Ala Ile His Cys Arg Ser Leu Ala Ser Gly Tyr His  
20 25 30  
Gly Leu Leu Pro Glu Gln Gln Ala  
35 40

<210> 492  
<211> 26  
<212> PRT  
<213> Homo sapiens

<400> 492  
His Glu Leu Thr Val Pro Ser Arg Met Gly Ser Lys Gly Lys Pro Tyr  
1 5 10 15  
Pro Cys Gly Phe Tyr Ser Ser Leu Ile Pro  
20 25

210

&lt;210&gt; 493

&lt;211&gt; 103

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 493

Lys Cys Ile Tyr Pro Lys Pro Ala Arg Thr His His Cys Ser Ile Cys  
 1 5 10 15

Asn Arg Cys Val Leu Lys Met Asp His His Cys Pro Trp Leu Asn Asn  
 20 25 30

Cys Val Gly His Tyr Asn His Arg Tyr Phe Phe Ser Phe Cys Phe Phe  
 35 40 45

Met Thr Leu Gly Cys Val Tyr Cys Ser Tyr Gly Ser Trp Asp Leu Phe  
 50 55 60

Arg Glu Ala Tyr Ala Ala Ile Glu Lys Met Lys Gln Leu Asp Lys Asn  
 65 70 75 80

Lys Leu Gln Ala Val Ala Asn Gln Thr Tyr His Gln Thr Pro Pro Pro  
 85 90 95

Thr Phe Ser Phe Arg Glu Arg  
 100

&lt;210&gt; 494

&lt;211&gt; 38

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 494

Ala Arg Gly His Trp Asn Leu Ile Leu Ile Val Phe His Tyr Tyr Gln  
 1 5 10 15

Ala Ile Thr Thr Pro Pro Gly Tyr Pro Pro Gln Gly Arg Asn Asp Ile  
 20 25 30

Ala Thr Val Ser Ile Cys  
 35

211

<210> 495  
 <211> 33  
 <212> PRT  
 <213> Homo sapiens

<400> 495  
 Trp Gln Cys Glu Leu Asp Cys Val Ser His Asp Ser Ser Thr His Ser  
     1                    5                    10                    15  
 Ala Pro Tyr Val Ile Ser Arg Ala Ser Lys Gly Ser Phe Ser Gln Asn  
                     20                    25                    30

Pro

<210> 496  
 <211> 83  
 <212> PRT  
 <213> Homo sapiens

<400> 496  
 Ser Lys Arg Ala Ser Gly Pro Ala Leu Gly Tyr His Ala Gly Gln Phe  
     1                    5                    10                    15  
 Lys Asp Gln Pro Phe Tyr His Cys Arg Arg Lys Thr Gln Cys Gly Glu  
                     20                    25                    30  
 Ile Leu Gly Leu Thr Ser Leu Tyr Ser Gly Lys Gln Lys Phe Gln Pro  
                     35                    40                    45  
 Gln Thr Arg Gly Gln Ala Ala Ser Tyr Leu Pro Cys Pro Val Leu Thr  
                     50                    55                    60  
 Arg Thr Ser Ser Arg Ile Gln His Trp Ser Trp Pro Pro Pro Leu Leu  
     65                    70                    75                    80  
 Leu Ala Val

212

<210> 497  
 <211> 31  
 <212> PRT  
 <213> Homo sapiens

<400> 497  
 Glu Ser Leu Gln Leu Arg Leu Leu Gly Gln Leu Glu Gly Ile Pro Gly  
 1 5 10 15  
 Cys Gly Tyr Arg Lys Ala Leu Ala Tyr Ser Gly Ala Leu Thr Phe  
 20 25 30

<210> 498  
 <211> 66  
 <212> PRT  
 <213> Homo sapiens

<400> 498  
 Ser Leu Ala Pro Trp Glu Trp Asn Glu Leu Gly Ala Pro Ser Leu Gly  
 1 5 10 15  
 Asp Cys Ser Leu Ser Leu Cys Asp Gly Ser Val Ser Trp Thr Val Ser  
 20 25 30  
 Ala Thr Thr Arg Ala Leu Ile Leu Leu Pro Met Leu Phe Gln Gly Pro  
 35 40 45  
 Pro Arg Ala Ala Phe Leu Arg Ile Leu Asp Gln Lys Glu Pro Val Gly  
 50 55 60  
 Leu Pro  
 65

<210> 499  
 <211> 72  
 <212> PRT  
 <213> Homo sapiens

<400> 499  
 Thr Ala Thr Leu Asn Ser Phe Phe Gly Gly Trp Gly Leu Ala Leu Leu  
 1 5 10 15  
 Leu Arg Leu Glu Cys Ser Asp Thr Ile Met Asp His Cys Ser Leu Asp  
 20 25 30  
 Leu Leu Gly Ser Ser Asn Pro Pro Ala Ser Ala Ser Gln Val Val Gly  
 35 40 45  
 Thr Thr Gly Ala Arg His His Ala Gln Leu Ile Phe Cys Phe Phe Val  
 50 55 60  
 Gln Thr Arg Ser His Ser Val Ala

65

70

&lt;210&gt; 500

&lt;211&gt; 47

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 500

Met Asp His Cys Ser Leu Asp Leu Leu Gly Ser Ser Asn Pro Pro Ala  
 1 5 10 15

Ser Ala Ser Gln Val Val Gly Thr Thr Gly Ala Arg His His Ala Gln  
 20 25 30

Leu Ile Phe Cys Phe Phe Val Gln Thr Arg Ser His Ser Val Ala  
 35 40 45

&lt;210&gt; 501

&lt;211&gt; 14

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 501

Gly Val Leu Lys Gln Ser Ser His Leu Val Leu Ser Lys Gly  
 1 5 10

&lt;210&gt; 502

&lt;211&gt; 21

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 502

Asp Tyr Ser Cys Glu Ser Leu Cys Pro Ala Leu Leu Ser Ile Ala Pro  
 1 5 10 15

Asp Ile Val Leu Asn  
 20

214

<210> 503  
 <211> 27  
 <212> PRT  
 <213> Homo sapiens

<400> 503  
 Thr Thr Ile His Lys Thr Gln Leu Gly Ser Tyr Lys Ile Leu Trp Glu  
 1 5 10 15  
 Pro Lys Glu Gly Tyr His Asn Ser Thr Trp Ile  
 20 25

<210> 504  
 <211> 9  
 <212> PRT  
 <213> Homo sapiens

<400> 504  
 Ile Arg Glu Ile Phe Leu Arg Arg Pro  
 1 5

<210> 505  
 <211> 24  
 <212> PRT  
 <213> Homo sapiens

<400> 505  
 Leu Lys Phe Gln Lys Pro Gly Lys Ile Gln Met Arg Gly Gly Gly Arg  
 1 5 10 15  
 Val Phe Trp Tyr Lys Asn Cys Lys  
 20

<210> 506  
 <211> 30  
 <212> PRT  
 <213> Homo sapiens

<400> 506  
 Asn Ser Ala Arg Val Thr Gln Lys Gly Glu Ser Val Gly Ser Val Gly  
 1 5 10 15  
 Cys Met Arg Ala Ile Ala Gly Phe Asp Asn Tyr Pro Leu Phe  
 20 25 30

<210> 507  
<211> 33  
<212> PRT  
<213> Homo sapiens

<400> 507  
Gly Thr Ile Gly Ile Phe Trp Pro Leu Pro Val Ala Ile Leu Ser Ser  
1 5 10 15

Gly Asp Tyr Leu Gln Thr Gln Ile His Arg Pro Leu Leu His Arg Gly  
20 25 30

Thr

<210> 508  
<211> 20  
<212> PRT  
<213> Homo sapiens

<400> 508  
Leu Pro Leu Pro Leu Ser Ser Leu Leu His Ile Ala Thr Cys Asn Pro  
1 5 10 15

Phe Pro Lys Thr  
20

<210> 509  
<211> 46  
<212> PRT  
<213> Homo sapiens

<400> 509  
Ser Tyr Phe Phe Val Tyr Asn Leu Ile Leu Lys Ile Ile Gln Gly Asp  
1 5 10 15  
His Ala Ser Ile Ile Leu Leu Ala Thr Ile Pro Ile Phe Gly Asp Ile  
20 25 30  
Tyr Tyr Val Lys Gly Gln Leu Ala Ser Phe Gly Pro Tyr Leu  
35 40 45

<210> 510  
<211> 21  
<212> PRT  
<213> Homo sapiens

<400> 510  
Leu Phe Tyr His Leu Glu Ile Ile Ser Arg His Lys Ser Ile Ala His  
1 5 10 15  
Cys Ser Ile Glu Ala  
20



217

<210> 511  
<211> 12  
<212> PRT  
<213> Homo sapiens

<400> 511  
Cys Ser Cys His Cys Pro Ser Arg Ala Phe Ser Thr  
1 5 10

<210> 512  
<211> 29  
<212> PRT  
<213> Homo sapiens

<400> 512  
Pro His Ala Ile His Ser Gln Lys Pro Ser Ser Ile Phe Leu Ile Thr  
1 5 10 15

Asp Val Phe Pro Asp Pro Pro Val Gly Ile Tyr Leu Leu  
20 25

218

&lt;210&gt; 513

&lt;211&gt; 48

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 513

Arg Lys Leu Phe His Lys Ile Asn Ser Lys Ser Phe His Leu Ser Gly  
1 5 10 15

Met His Ile Leu Ile Ser Val Trp Ile Val Arg Ser Arg Ile Ile Lys  
20 25 30

Val Lys Tyr Glu Leu Leu Leu Cys Phe Phe Asp Val Ile Phe Tyr Val  
35 40 45

&lt;210&gt; 514

&lt;211&gt; 41

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 514

Asn Ser Ala Arg Asp Val Phe Phe Thr Gln Lys Ile Leu Tyr Ser Gln  
1 5 10 15

Thr Cys Ile Phe Phe Pro Cys Leu Val Pro Phe Ser Phe Leu Phe Ser  
20 25 30

Phe Phe Phe Phe Leu Ser Phe Val Gly  
35 40

&lt;210&gt; 515

&lt;211&gt; 56

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 515

Met Phe Ser Ser Leu Lys Lys Phe Tyr Ile Leu Lys His Val Tyr Ser  
1 5 10 15

Phe Pro Val Leu Phe His Phe Leu Phe Phe Phe Leu Phe Ser Phe Ser  
20 25 30

Phe Leu Ser Trp Ala Glu Lys Gly Ala Gly Lys Met Lys Leu Ala Thr  
35 40 45

Glu Asn Cys Lys Met Val Lys Ser  
50 55

220

&lt;210&gt; 516

&lt;211&gt; 39

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 516

Ile Gln Leu Leu Tyr Leu Lys Gly Ala Ala Met Lys Tyr Leu Ser Tyr  
1 5 10 15

Val Ala Arg Leu Leu Phe Leu Lys Ala Leu Asp Leu Phe Ala Pro Lys  
20 25 30

Met Val Gln Ile Asp Ser Phe  
35

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US98/13684

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(6) : C07H 21/04; C12N 15/63

US CL : 536/23.5; 435/69.1, 172.3, 320.1, 325

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 536/23.5; 435/69.1, 172.3, 320.1, 325

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

GENBANK, EMBL, SWISSPROT, PIR, GENESEQ, USPTO nucleotide and polypeptide databases  
search terms: SEQ ID NO: 11-20, 150-159

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE Genbank, US National Library of Medicine, (Bethesda, MD, USA), No. G15147, MEYERS, R.M. 'Human STS SHGC-15725', complete record, 04 January 1996.	1, 7-10, 14
X	Database Genbank, US National Library of Medicine, (Bethesda, MD, USA), No. AA398986, HILLIER et al. 'WashU-Merck EST Project 1997', complete record, 16 May 1997.	1, 7-10, 14
X	Database Genbank, US National Library of Medicine, (Bethesda, MD, USA), No. AA044254, HILLIER et al. 'The WashU-Merck EST Project', complete record, 04 September 1996.	1, 7-10, 14

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
*A* document defining the general state of the art which is not considered to be of particular relevance	*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
*B* earlier document published on or after the international filing date	*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
*L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*A* document member of the same patent family
*O* document referring to an oral disclosure, use, exhibition or other means	
*P* document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search 24 SEPTEMBER 1998	Date of mailing of the international search report 22 OCT 1998
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer SCOTT D. PRIEBE Telephone No. (703) 308-0196

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US98/13684

## C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Database Genbank, US National Library of Medicine, (Bethesda, MD, USA), No. AA327382, ADAMS et al., 'Initial assessment of human gene diversity and expression patterns based upon 83 million nucleotides of cDNA sequence', complete record, 20 April 1997.	1, 7-10, 14
X	Database Genbank, US National Library of Medicine, (Bethesda, MD, USA), No. R06009, HILLIER et al. 'The WashU-Merck EST Project', complete record, 03 April 1995.	1, 7-10, 14
X	Database Genbank, US National Library of Medicine, (Bethesda, MD, USA), No. H55089, TROFATTER et al. 'An expression-independent catalogue of genes from human chromosome 22', complete record, 07 December 1995.	1, 7-10, 14
X	Database Genbank, US National Library of Medicine, (Bethesda, MD, USA), No. W05747, HILLIER et al. 'The WashU-Merck EST Project', complete record, 23 April 1996.	1, 7-10, 14
X	Database Genbank, US National Library of Medicine, (Bethesda, MD, USA), No. T66050, HILLIER et al. 'The WashU-Merck EST Project', complete record, 07 March 1995.	1, 7-10, 14.
X	GORBULEV et al. Organization and chromosomal localization of the gene for the human bombesin receptor subtype expressed in pregnant uterus. FEBS Letters. 1994, Vol. 340, pages 260-264, especially pages 260-261, 'Materials and Methods', and page 262, Fig. 1.	1, 7-10, 14
X	DATABASE Genbank, US National Library of Medicine, (Bethesda, MD, USA), No. X67209, GALIANA et al. 'Proliferation and differentiation properties of bipotent glial progenitor cell lines immortalized with the adenovirus E1A gene', complete record, 19 February 1994.	1, 7-10, 14

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## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2. ☐ Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
  
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
  
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  
1-10,14,15,21

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.  
☐ No protest accompanied the payment of additional search fees.

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### BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING

This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1.

Group I, claim(s) 1-10, 14, 15 and 21, drawn to polynucleotides comprising SEQ ID NO: X or encoding SEQ ID NO: Y or a cDNA in the material deposited with American Type Culture Collection with accession number Z, wherein the cDNA encoding Y or in Z hybridizes to X; vectors comprising the polynucleotide; and cells comprising the polynucleotide or the vector or that express the polypeptide. Additionally, Group I contains the first method of using the cells to make a product (claim 15). There are a total of 138 polynucleotide sequences of which the first ten (10) are selected for examination and therefore, there are an additional thirty-two (32) remaining additional groups of four (4) polynucleotide sequences.

Group II, claim(s) 11, 12, 16, 23, drawn to polypeptides or fragments thereof with the amino acid sequence of SEQ ID NO: Y as found in the material deposited with American Type Culture Collection with accession number Z. There are 137 additional polypeptides, and therefore, there are an additional 137 remaining additional groups of polypeptides.

Group III, claim(s) 13, drawn to an antibody or fragments thereof that bind to a polypeptide with the amino acid sequence defined by SEQ ID NO: Y as found in the material deposited with American Type Culture Collection with accession number Z. There are 137 additional antibodies that bind to an additional 137 polypeptides, and therefore, there are an additional 137 remaining additional groups of antibodies.

Group IV, claim 17, drawn to a process of preventing, treating, or ameliorating a medical condition by administering a polypeptide or polynucleotide, which is a second alternative use of the first claimed product in Group I. In group IV, and where additional fees are paid, the claims are searched only insofar as they are applicable to the selected polypeptide and its corresponding SEQ ID NO as the first invention as directed to a process practiced using a polypeptide. The second invention is the practice of the process using a polynucleotide. In each instance, the same selected polypeptide as for the first invention of Group II or for the first 10 polynucleotides of Group I would be examined. Applicant may elect to pay additional fees for each additional polypeptide beyond the first or for each additional four (4) polynucleotides after the first ten (10), as indicated above with respect to Groups I and II.

Group V, claim 18, drawn to a method of diagnosis of a pathological condition based on a polynucleotide, an additional alternative process for using the first claimed product of Group I. Additionally, there are an additional thirty-two (32) remaining additional groups of four (4) polynucleotide sequences which constitute an additional 32 inventions beyond the first of using one of the first 10 polynucleotides.

Group VI, claim 19, drawn to a method of diagnosis of a pathological condition based on a polypeptide, an additional alternative process for using the first claimed product of Group II. Additionally, there are an additional 137 remaining additional groups of one (1) polypeptide each which constitute an additional 137 inventions beyond the first of using the first polypeptide.

Group VII, claim 20, drawn to a method of identifying a binding partner for a polypeptide. There are 137 additional polypeptides, and therefore, there are an additional 137 remaining additional inventions of processes using the polypeptides.

Group VIII, claim 22, drawn to a method of identifying a biological activity of a polypeptide, another additional, alternative use of the product of Group I. Additionally, there are an additional thirty-two (32) remaining additional groups of four (4) polynucleotide sequences which constitute an additional 32 inventions beyond the first of using one of the first 10 polynucleotides.

The inventions listed as Groups I through VIII do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons.

Claims of Groups I, IV (drawn to use of polynucleotides), V and VIII are drawn to polynucleotides, polynucleotide constructs or methods requiring the use of same that contain more than ten (10) individual, independent and distinct nucleotide sequences in alternative form. Accordingly, these claims are subject to lack of unity as outlined in 1192 O.G.



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68 (19 November 1996). The first ten (10) individual polynucleotide sequences designated as "X" in the table on pages 143-153 of the description selected by applicant are included for search. The corresponding SEQ ID NO: Y and ATCC accession number for "Z" for each selected "X" should be noted. The search of no more than ten sequences may include the complements of the selected sequences and, where appropriate, may include subsequences within the selected sequences, e.g. probes or primers.

Where applicant may elect to pay additional fees for a search of sequences beyond the initial ten (10) selected polynucleotide sequences, and in accordance with 1192 O.G. 68 (19 November 1996), applicant may select additional groups of polynucleotides consisting of four (4) sequences beyond the additional ten (10) sequences for search with Group I. Applicant may also pay additional fees for search of Groups IV, V and VIII, wherein the ten initial polynucleotides selected for Group I will be searched. For search of additional groups of four polynucleotide sequences in Groups IV, V, and VIII selected for search in Group I, applicant must pay additional fees also to have the additional methods of use for the additional groups of four (4) polynucleotides selected searched with Group I. For example, if applicant elects to have 14 (10 + 4) sequences searched for Groups I and IV, fees would be paid for three additional inventions, the first selected group of 4 polynucleotides in group I, the use of initial ten polynucleotides in Group IV and the use of the additional four polynucleotides in Group IV.

As to the polypeptides of Groups II or used in III and IV (drawn to use of a polypeptide), VI and VII, each individual polypeptide is a different protein. Should additional fees be paid for search of Groups II, III, IV, VI or VII be paid, the amino acid sequence corresponding to the first polynucleotide sequence selected by applicant for Group I will be searched with the additional group(s) for which additional fees are paid. Applicant may select additional proteins or antibodies to be searched by specifying the appropriate SEQ ID NO: Y corresponding to a selected polynucleotide sequence of Group I. If additional fees are paid more than one of Groups II, III, IV, VI or VII, search of additional polypeptides than the initial one (1) polypeptide would require additional fees for each additional polypeptide selected for search with each additional group of Groups II, III, IV, VI or VII.

The SEQ ID NOs of Groups I, IV, V, and VIII encode, absent evidence to the contrary, structurally and functionally distinct polypeptides, with different chemical, physical and biological properties. For example see the description of the different genes 1 to 123 on pages 5 to 142 of the description. Each are directed to genes encoding different proteins, expressed in different cells, and mapping to different chromosomes, and are therefore distinct and different polynucleotides not sharing any special technical feature. Likewise, each of the polypeptides of Group II, IV, VI and VII and antibodies of Group III is a distinct and different protein, not sharing any special technical feature.

Each of Groups IV to VII are directed to alternative processes of using the products of Groups I or II. Also, in so much as each group encompasses a multitude of different inventions *vis a vis* the different polynucleotides or polypeptides, each group fails to share the same special technical features throughout the scope of each group.